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EXPERIMENTAL SURGERY OF THE THORACIC OESOPHAGUS

By ROBERT T. MILLER, JR., and W. D. W. ANDRUS

(From the Surgical Department of the Johns Hopkins University and Hospital)

The announcement, about twenty years ago, of a method of control of respiratory pressures brought the chest within the realm of elective surgery and was followed by much experimental work dealing with surgery of the thoracic viscera. A number of the workers concerned themselves with surgical problems of the œsophagus, in particular with resection and suture, and for a time there seemed reason to hope for a considerable advance in this field. But the expected results have not been forthcoming. Œsophageal surgery has not yet emerged from the experimental phase of its development.

Perhaps the thing most sought for has been a satisfactory operative method for meeting the problem offered by carcinoma, particularly of the lower third of the tube. In general, two schools have developed; one of them, influenced by the high infection risk, attempts, by mobilizing the œsophagus, to convert the operation into an extrathoracic procedure, while the other, striving for simplicity, attempts the suture *in situ.* The extrathoracic method has but very rarely resulted in restoration of an intact tube and never in less than three months; most of the cases have been in the hands of the surgeon nine months or more, which fact, together with the very small chance of definitive cure, throws grave doubt upon the value of the method. In contrast with it, one inevitably thinks of the relative surgical simplicity and the prompt functional result that would be offered by intrathoracic suture, if such were possible, and with this in mind we thought it worth while to attempt again to devise an intrathoracic method of operation applicable to strictures of the œsophagus in man. We feel a certain degree of encouragement from our efforts as far as they have gone and therefore offer this report.

Review of Intrathoracic Suture to 1922

The first successful intrathoracic suture of a resected œsophagus was made by Dobromysslow,[1] working in Tomsk in 1901; after a 4 cm. resection in the lower third of the œsophagus of a dog, the ends were united by two rows of silk sutures and at autopsy three weeks later there was found satisfactory healing with slight dilatation of the œsophagus proximal to the suture. In 1905 Sauerbruch [2] made a lengthy report of experimental and clinical work. In general, end-to-end suture after resection met with little success and failed uniformly after resection of 7 cm. or more, because of tension. He tried to avoid tension by freeing the cardia from the diaphragm and anastomosing to a tip of the stomach drawn into the pleural cavity; in 20 attempts he succeeded 3 times in obtaining healing. Six attempts were then made to obtain union by implanting the upper œsophageal end in the stomach after the fashion of a Witzel gastrostomy; the suture failed in all 6. It is interesting to note that recently Kirschner [3] has again proposed the Witzel-like method because of the poor healing power of the œsophagus. Although mobilization of the stomach did away with tension on the suture line, the stitch still tore out; this fact together with the danger of infection led Sauerbruch to propose his two-stage plan of resection of low œsophageal growths, the first operation to be a thoracotomy, freeing the growth without opening the tract and invaginating the growth into the stomach, the second operation to be a laparotomy, opening the stomach and amputating the invaginated tumor. The almost uniform regularity with which his stitch, however modified, tore out of the œsophagus led Sauerbruch to try the Murphy button, which proved so much more successful than suture in his hands that he adopted it as the method of choice and abandoned any further attempts with suture.

Four years later Willy Meyer [4] reported on the subject. He pulled enough of the stomach into the chest to permit anastomosis by suture and in 6 attempts obtained 2 functioning anastomoses. About the same time Zaaijer [5] reported 3 successes in 8 attempted œsophageal sutures and Janeway and Green [6] published some experimental work upon the basis of which they were inclined to favor the Murphy button in preference to suture.

In 1913 Omi [7] of the Dairen Hospital in South Manchuria reported some excellent work. He used silk sutures and placed them in three layers, the first in the mucosa, the second in the muscle and adventitia, the third layer being an external continuous Lembert. Of 9 end-to-end sutures of the thoracic œsophagus 7 were successful; of 5 intrathoracic œsophagogastrostomies 3 showed intact suture lines, one animal dying of diaphragmatic hernia on the 5th day, one of pneumonia on the 62d day and one, sacrificed on the 135th day, showing a large diaphragmatic hernia at autopsy. Omi then attempted gastrectomy followed by anastomosis between the œsophagus and the duodenum or jejunum and in 11 animals obtained an intact suture line 7 times, the results being controlled by autopsy. Finally, he attempted resection and immediate reimplantation of 4-6.5 cm. lengths of the œsophagus, but the transplant uniformly became gangrenous. Omi felt that a carefully made suture of the œsophagus is sufficiently reliable to warrant its adoption in human surgery; beyond question his work justified this conclusion if the result of suture in the dog may be accepted as applicable to man.

In 1914 Enderlen [8] reported the result of four years' work on œsophageal suture. His main effort was directed toward devising some way of restoring the continuity of the tube after extensive œsophageal resections, but his first success came, as with Omi and Zaaijer, in end-to-end suture after resections of but 3 cm. Efforts to restore the continuity of the tract after extensive resections by substituting for the œsophagus either a loop of small bowel, or a *Jianu* [9] tube made from the greater curvature of the stomach, uniformly resulted in gangrene of the substituted material. Mobilization of the proximal portion of the œsophagus to a dorsal extrathoracic position for eventual anastomosis with a *Jianu* tube brought out through the chest-wall resulted in necrosis of the end of the œsophagus. Enderlen's final effort was made with the stomach; after gastro-enterostomy placed in the fundus rather than the antrum the stomach was mobilized except for the left side, the pylorus divided and pulled up through the chest to the neck where it was anchored to the skin above the clavicle. This arrangement invariably resulted in dilatation of the stomach so great as to produce fatal compression of the heart and lungs.

It is noteworthy that among these men Sauerbruch is almost alone in adopting the Murphy button in place of sutures and that he came to this view after persistent efforts to suture the œsophagus had convinced him that the stitch, no matter how made, is almost certain to tear out. In spite of his adoption of the Murphy button, however, the advice in its favor has had little heed, for almost all experimenters have persisted in efforts with the suture which, as a result, has been brought to a reasonable degree of security. In the literature of this subject one finds frequent expression of the opinion that suture of the œsophagus is uncertain because of three factors, viz., the œsophagus offers no firm tissue for the suture to grasp and hence it tears out; it is difficult to avoid a fatal degree of tension on the suture line, and finally, freeing enough of the tube to allow room for suture is apt to destroy circulation to the point of resultant gangrene. Our work has convinced us of the fallacy of this opinion. The submucosa of the dog's œsophagus is so strong and so well developed that it offers, at least in the lower third, as sturdy tissue for the suture to grip as does the bowel. In the lower third of the tube, tension on the suture line can be entirely avoided; furthermore, we believe a method is presented

whereby tension can be avoided for any suture of the dog's thoracic œsophagus excepting only that of the extreme upper portion. We have not encountered necrosis of the isolated tube.

Resection in the Lower Third of the Œsophagus Restoration of the Continuity

After resection in the lower third, continuity may be re-established by an end-to-end anastomosis of the œsophagus or by implanting the end of the œsophagus in the fundus of the stomach drawn up into the chest through the diaphragm. Unless the stomach is first mobilized by freeing it from the diaphragm and drawing it into the chest, end-to-end suture offers little chance to bridge any but a very short gap, and for this reason seems destined to play a small part in human surgery. Conversely, if the stomach is so mobilized and drawn into the chest, it is found that a wider gap can be bridged by implantation of the œsophageal end into the fundus than by end-to-end suture; this scheme, therefore, became our routine procedure. The bulkhead method of intestinal suture, recently described by the late Professor Halsted,[10] seemed particularly suitable for our purpose and was therefore adopted, although with a slight modification in that we did not use the knife described in his report.

The operation we practised is carried out by the following plan. After a preliminary dose of morphine, anæsthesia is maintained by ether insufflation. The approach is made through the 8th left intercostal space, which gives an excellent exposure. The lower third of the œsophagus, extending roughly from the diaphragm to the bifurcation of the trachea, is readily isolated; during this manœuvre the right pleural cavity may be opened. The two vagus trunks accompany the œsophagus closely, the right occupying an antero-lateral position and the left a postero-lateral; these two trunks can be easily freed and preserved at this level, but since it probably would be impossible to save them in resecting the cardia or lower œsophagus for carcinoma, we have usually divided them when first encountered. Separation of the cardia from the diaphragm is readily made by hugging the cardia closely and is followed by ligation of several vessels in the cut edge of the diaphragm, viz., those anastomosing the phrenic and coronary systems. The fundus of the stomach can now be drawn through the diaphragm without difficulty, and if one then doubly ligates and divides the trunk of the coronary artery, the entire stomach, with or without the spleen, can be drawn into the chest. The œsophagus is now divided at the cardia and the cardial stump inverted. The site for implantation is selected and prepared on the anterior wall of the stomach well up on the fundus to the left of the cardia. A circular area, the desirable diameter of which seems to be about twice that of the œsophageal lumen, is outlined by an incision through the muscular coat; this exposes numerous vessels which require ligation as was shown by one prompt post-operative death caused by hæmorrhage from this source. A temporary occluding ligature is obtained by threading a needle with strong silk and grasping the tissue in the bed of this incision at close intervals; this ligature catches preferably only the submucosa and must be tied snugly to prevent telescoping of the gastric mucosa. The lumen of the œsophagus is closed in similar fashion at the upper limit of the proposed resection. Both the stomach and œsophagus are now cut away just distal from the occluding ligatures and the resultant stumps are first sterilized with the cautery or carbolic acid and then brought into apposition by mattress sutures of fine silk; just before the last two or three mattress sutures are tied, the loop of each occluding ligature is drawn into plain view and cut, and these threads are pulled out, thus re-establishing the lumen. Care is taken to secure a firm hold on the submucosa with the first row of stitches. The second suture layer consists of a continuous stitch of fine silk which buries the first layer, grasping preferably only the muscular coats of the two viscera. The operation is completed by sewing the edge of the diaphragm to the stomach wall and closing the chest with a pericostal stitch. The method outlined is well illustrated by the accompanying pictures (Figs. 1-7).

Results of Operation

Anastomosis was made by the above method 18 times. Four dogs died within a few hours after operation of hæmorrhage and shock. Fourteen dogs survived operation; of this number 11 were shown to have an intact suture line and a functioning anastomosis. The fate of these 11 may be listed as follows: one lived 6 months and was sacrificed; 2 died of dilatation of the stomach on the 21st and 24th day, respectively; 4 died of distemper 3, 7, 17, and 20 days after operation, respectively; one died of diaphragmatic hernia on the 6th day; 3 died of infection on the 5th, 10th, and 19th day, respectively. Thus, among the 11 sutures which are classed as successful, one animal was in excellent health at the end of 6 months, 7 died of conditions reflecting in no way upon the security of the suture of the œsophageal wall, viz., distemper, dilatation of the stomach and diaphragmatic hernia, and 3 dogs dying of infection showed at autopsy a healed and functioning anastomosis (Figs. 8-13). This is a rather high incidence of infection, but we do not feel that it is prohibitive. It seemed evident to us, as our technique developed, that the infection risk could be reduced, and was in fact reduced, to a point approaching that of intestinal suture. Inasmuch as this report is submitted in order to demonstrate that a suture of the œsophagus can be so made as to hold securely and to result in satisfactory healing, the ultimate fate of our animals is without significance provided autopsy showed

an intact functioning anastomosis as it did in the 11 animals in question.

It is of interest to note that dilatation of the stomach has occurred in the work of others (Sauerbruch, Enderlen) and that it seems to be a result of disturbance of the neurological control of the stomach rather than of compression of the pylorus by the diaphragm which has been stitched about the distal part of the stomach. Some effort was made to associate it with section of the vagus nerves, but the problem proved so complicated that work upon this subject was temporarily abandoned. It seems reasonable to anticipate that prompt recognition and treatment of this possible postoperative complication in the human would meet the situation successfully, for there is some experimental evidence that the disturbance of neurological control, even if due to section of the vagus nerves, is not permanent and that the stomach will soon regain its tone. It was found that diaphragmatic hernia can be prevented by accurate stitching of the edge of the diaphragm to the stomach, but that this stitch must be made with great care; since the size of the human chest offers greater accessibility, it would seem that the repair should be easier and therefore more secure, thus reducing the hernia chance in man well below that in the dog. It is interesting to note that Omi, after trying a number of procedures in an effort to prevent hernia, completely excised the diaphragm on the left side and found that the animal seemed to suffer no marked consequences; he was led to attempt this through the observation of a Turkish soldier in the First Balkan War who lived an active military life for a number of years with a rather complete diaphragmatic hernia caused by a gunshot wound.

We feel that our experience, as detailed above, shows œsophageal suture to be entirely feasible upon the dog, that the high mortality was due to causes other than failure of the suture, and that these causes are in large measure avoidable.

Three of the fourteen tests failed; twice because the suture tore out as the result of tension, and once because of a small area of gangrene of that part of the stomach wall involved in the suture. Mobilization of the stomach, as developed in the later part of our work, offers an apparently secure means of avoiding tension, at least in the dog, so that failure of the suture from this cause is not to be anticipated under ordinary conditions. The one instance of gangrene of the wall of the stomach was not satisfactorily explained, though it seemed probably due in some way to an incorrectly placed suture which occluded a terminal artery; the fact that it occurred only once reduces its significance.

Mobilization of the Stomach

Experimental work has shown definitely that end-to-end suture of the dog's œsophagus to bridge a gap of more than 3 centimeters is apt to fail because of tension on the suture. This limits the possible usefulness of the operation greatly; in our present state of diagnostic ability one hardly need anticipate encountering an œsophageal carcinoma which could be satisfactorily treated by so limited a resection. It is obviously necessary to devise other means of substitution for that portion of the œsophagus removed. In an effort to solve this problem we experimented in mobilization of the stomach.

If, through an intercostal incision, one separates the cardia from the diaphragm, it is immediately possible to draw a portion of the stomach into the thorax, but the extent to which this may be done is definitely limited by the short and direct coronary artery, which first reaches the stomach on the lesser curvature near the cardia, and, to a lesser degree, by the vasa brevia entering from the splenic artery. Division of the coronary artery liberates the stomach greatly, allowing much more of it to be drawn into the chest; and if one sections the vasa brevia as well, it is found in the dog that the entire stomach can be drawn readily into the left pleural cavity and the edge of the diaphragm sutured to the pylorus without tension, thus providing more than enough material to replace the lower third of the œsophagus (Fig. 3). The distance to which the fundus of the dog's stomach can be carried into the upper chest after such a mobilization is fixed by the left gastro-epiploic artery which is the next structure to be drawn taut, but we have freed the stomach by this method many times and have found it possible in every instance to carry it quite high enough to replace the lower two-thirds of the thoracic œsophagus and frequently more (Fig. 14). Experiments were, therefore, undertaken to determine whether a stomach so treated is invariably viable. In 19 dogs we divided the anastomotic branches of the phrenic artery in the diaphragm about the cardia, the coronary artery and the vasa brevia, sometimes replacing the stomach in the abdomen and sometimes leaving it in the chest. Only one of the stomachs so treated showed any alteration in viability whatever, but this one case presented a definite necrosis of a limited portion of the fundus. If one carries the idea further and divides the left gastro-epiploic artery in addition to the three already sectioned, as we did in 15 instances, at least two-thirds of the stomachs so treated show quite promptly an area of necrosis in the fundus 3 to 4 cm. in diameter, involving the entire thickness of the wall and resulting in acute perforating ulcer (Figs. 15-17). Obviously the stomach wall will not withstand so wide a destruction of its vascular supply.

In a report unknown to us until our work on mobilization of the stomach was about completed, we found a proposal by Kirschner [3] of much the same scheme. His idea is to separate the stomach freely from its attachments, leaving only the blood supply entering from the right side, and to utilize it in an extrathoracic reconstructive operation. Kirschner supports his proposal by citing a statement from Litthauer [11, 12] that one-third of the circu-

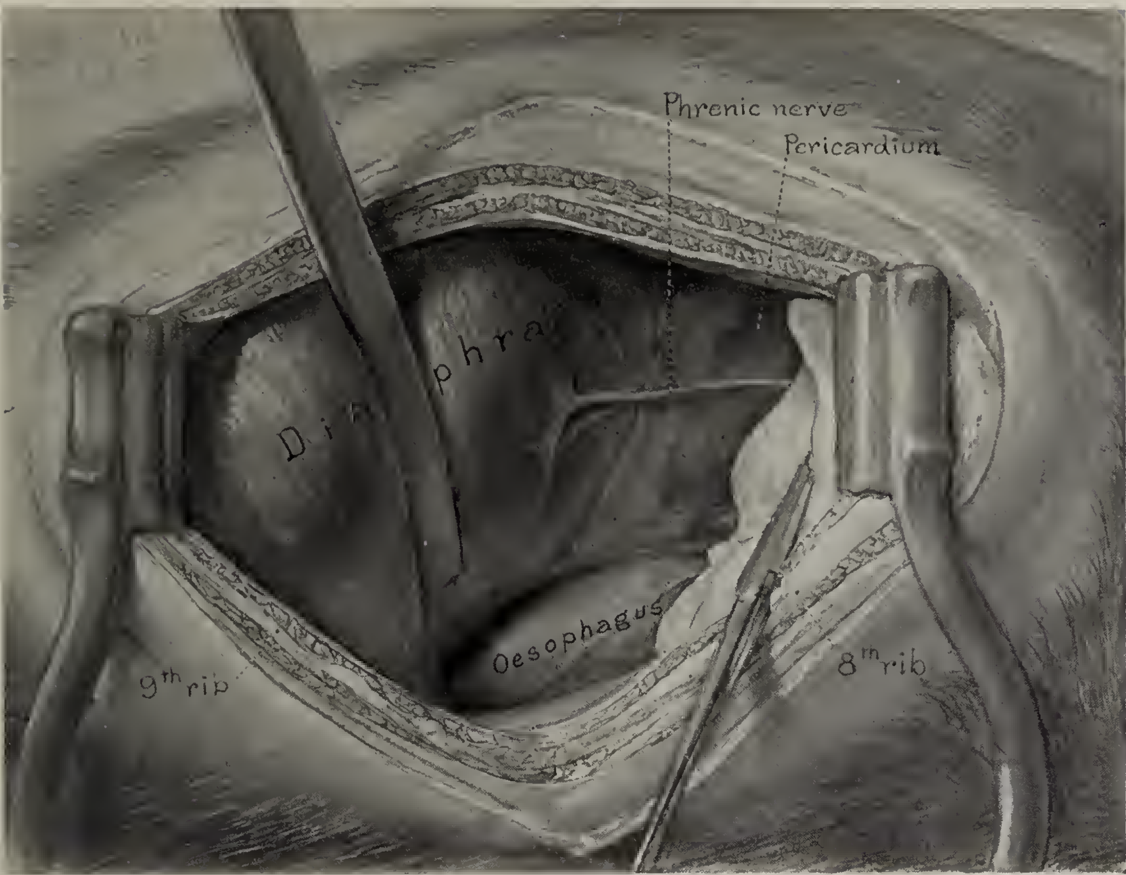

Fig. 1.—Illustrates the approach through the 8th left intercostal space.

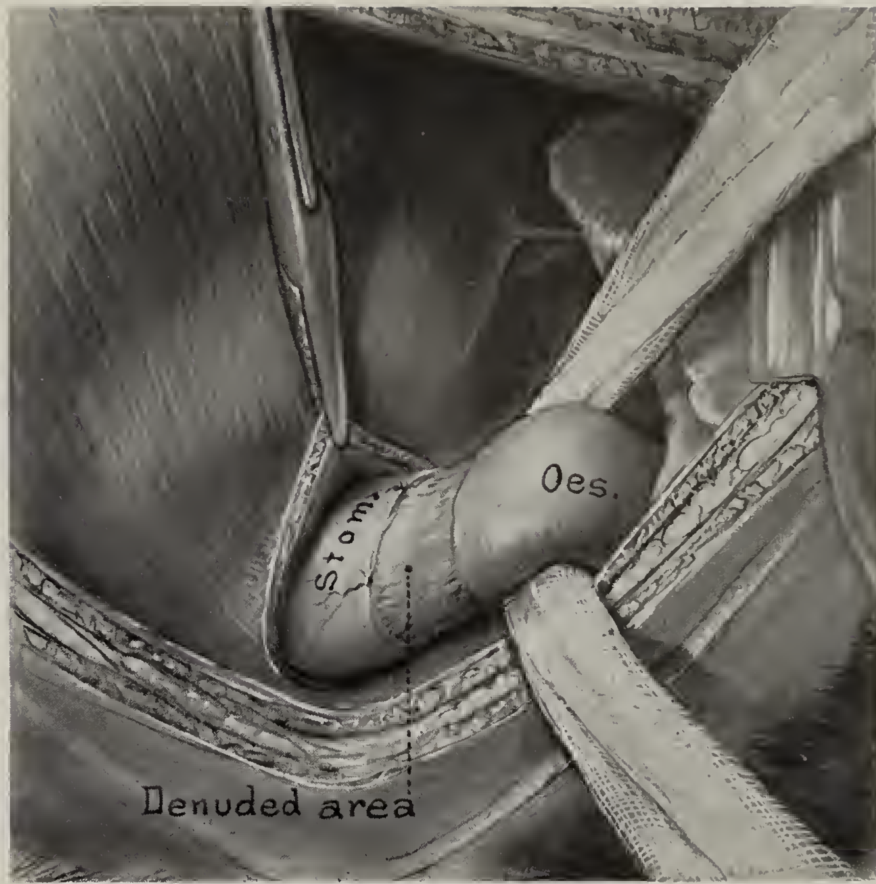

Fig. 2.—Separation of the cardia from the diaphragm completed.

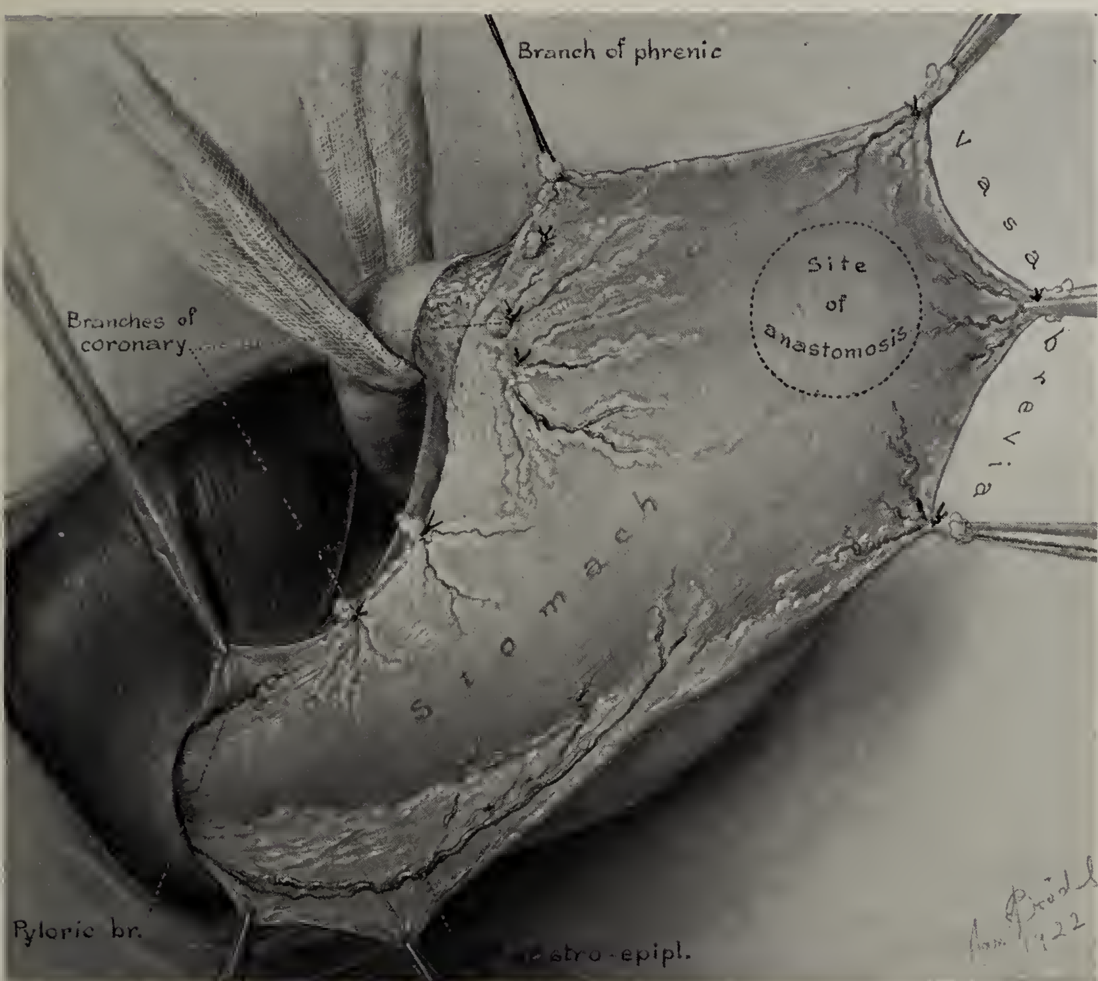

Fig. 3.—Stomach drawn into left pleural cavity after ligation of the vessels in the diaphragm, the coronary artery and the vasa brevia. Note the entire stomach drawn into the chest.

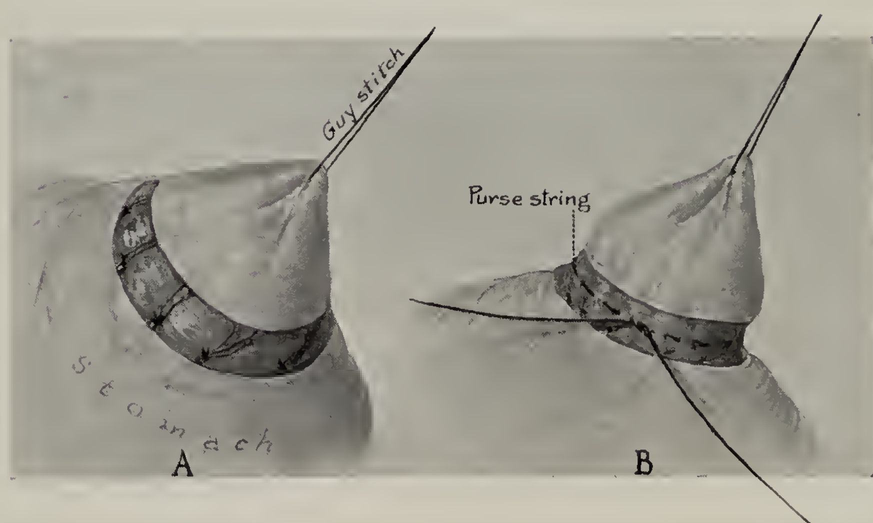

Fig. 4.—Preparation of the site for implantation in the stomach wall.

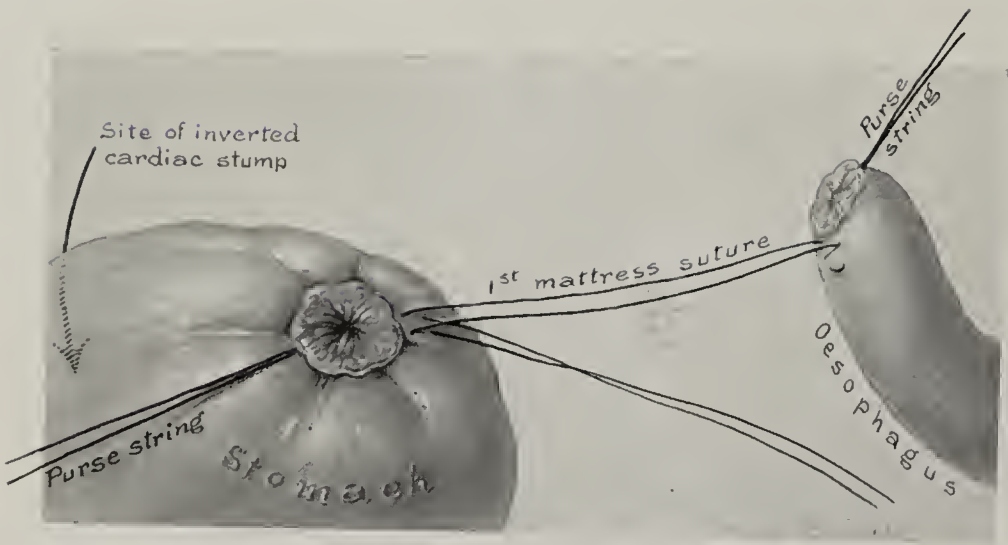

Fig. 5.—Beginning of the stitch anastomosing the oesophagus to the stomach.

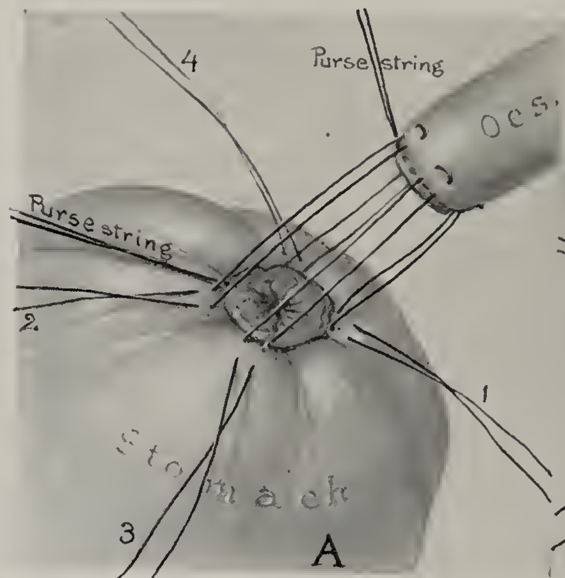

Fig. 6A.—The four cardinal mattress stitches have been placed.

Fig. 6B.—The first layer is complete except for tying the two final sutures.

Fig. 7A.—The first layer completed.

Fig. 7B.—Placing of the second and final suture layer.

Fig. 8.—Suture line of dog dead on 5th day of diaphragmatic hernia. Anastomosis seen from peritoneal aspect. The stomach wall immediately around the anastomosis has been excised and spread flat. From this surface the stump of the oesophagus projects directly toward the observer, thus bringing practically the entire suture line into view.

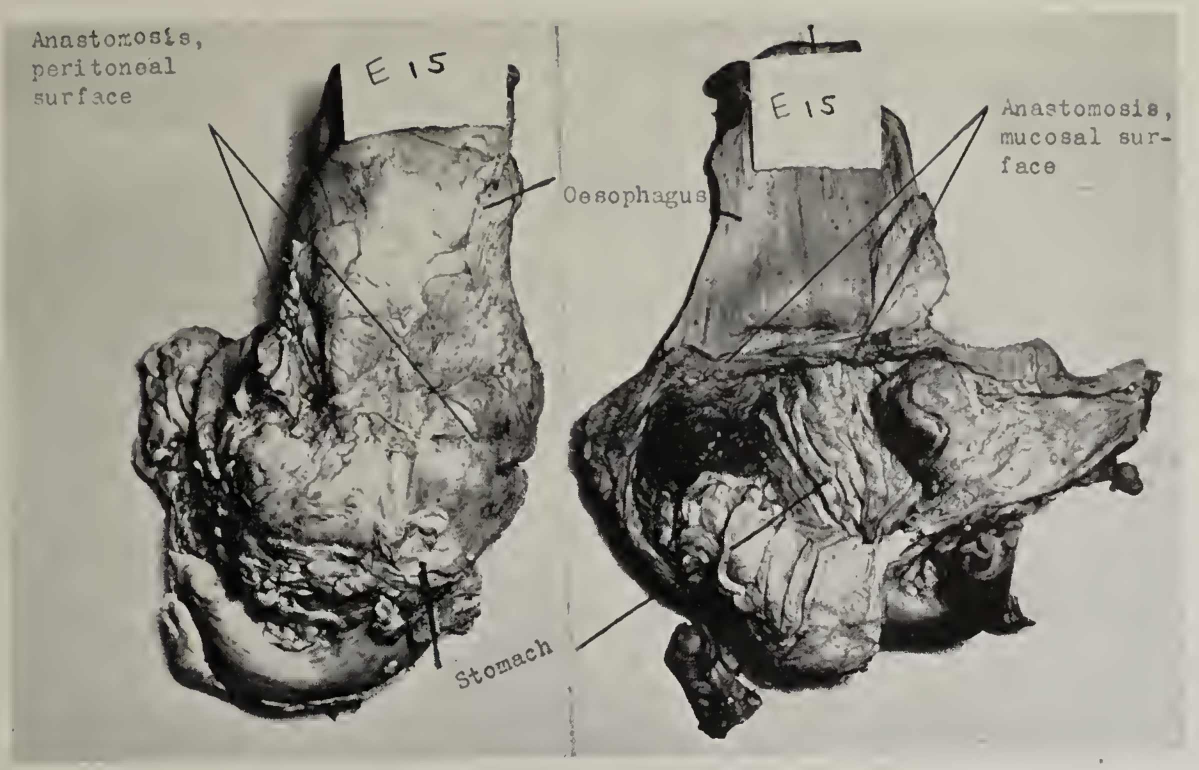

Fig. 9.—Suture line of dog dead on 10th day of infection.

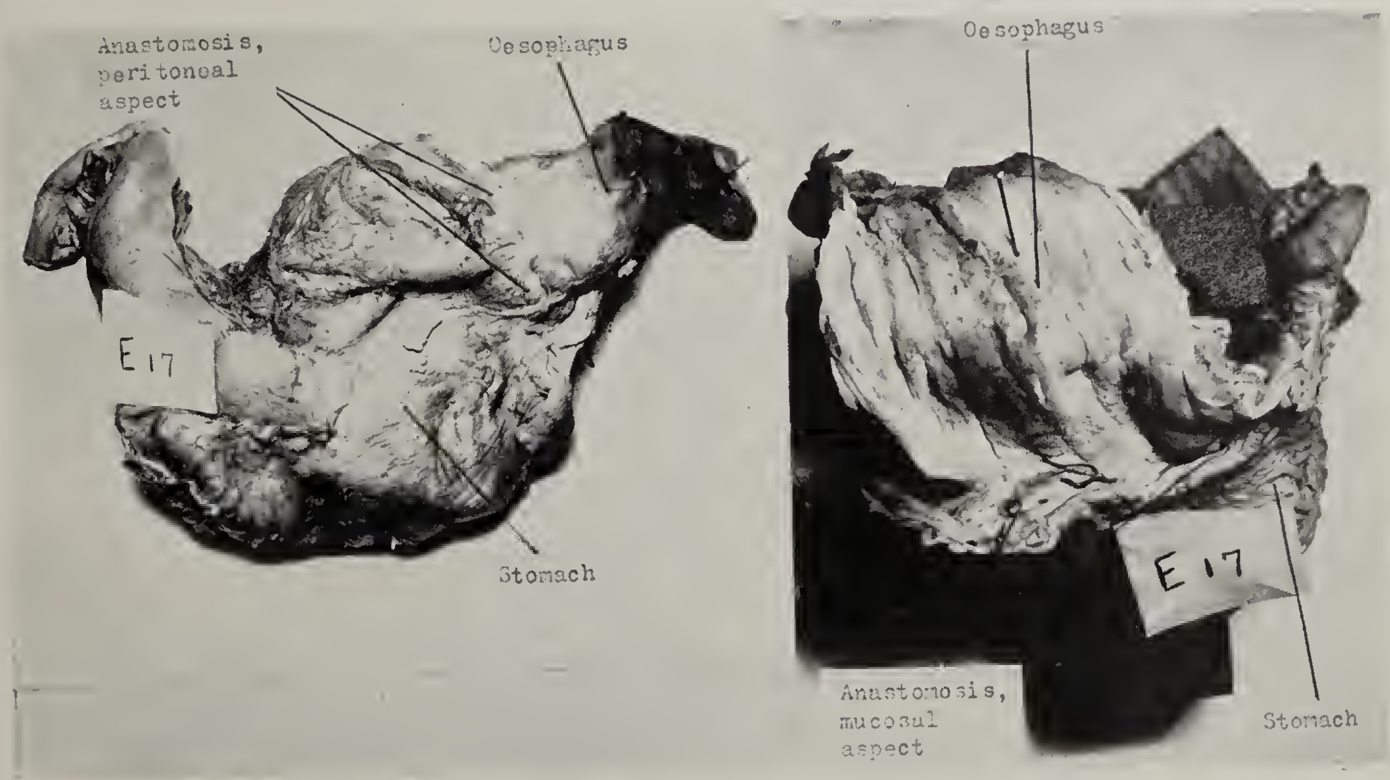

Fig. 10.—Dog dead on 24th day of dilatation of stomach compressing heart and lungs. Site of anastomosis. Note silk stitch hanging free in the lumen.

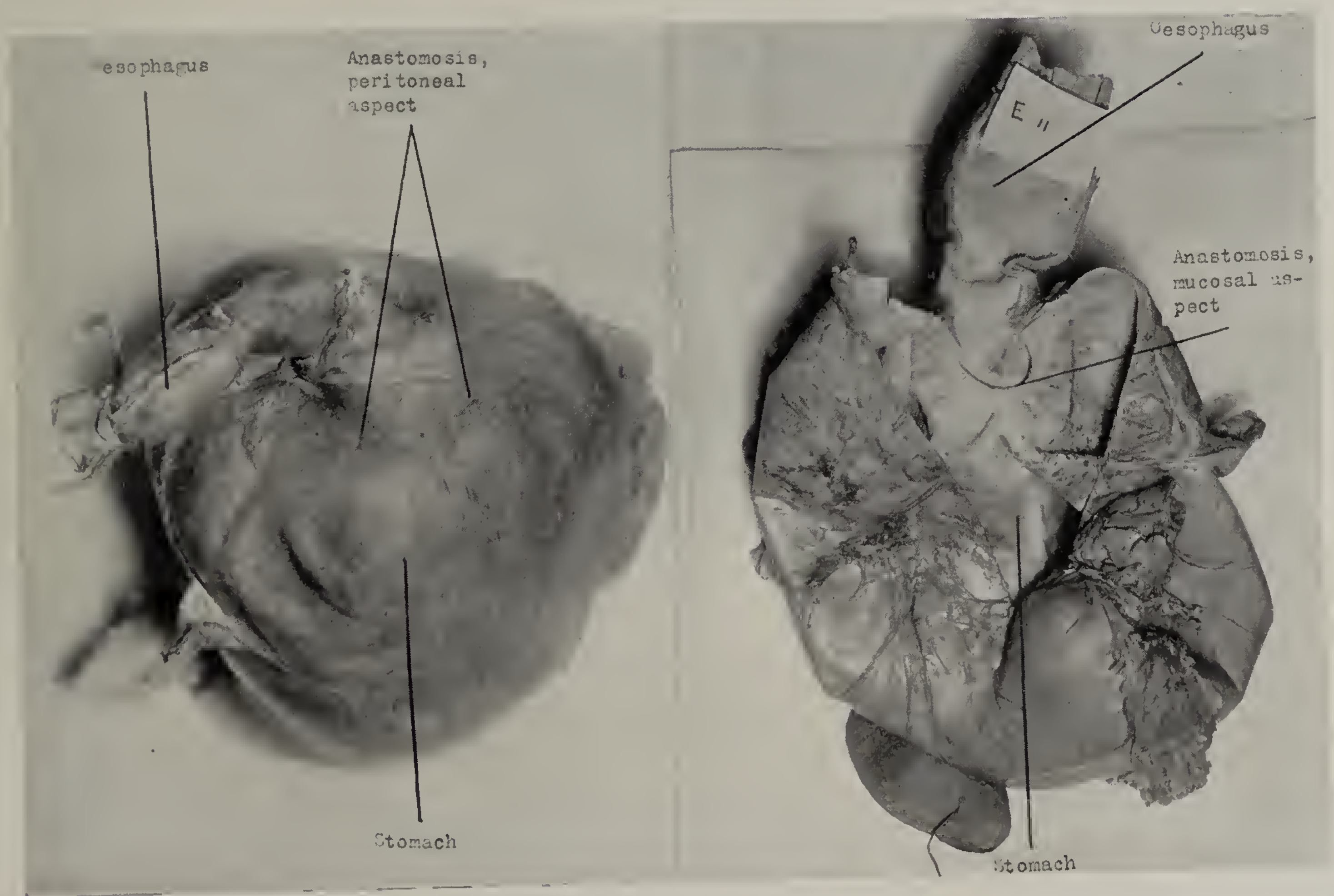

Fig. 11.—Dog dead on 21st day of gastric dilatation compressing heart and lungs. Site of anastomosis.

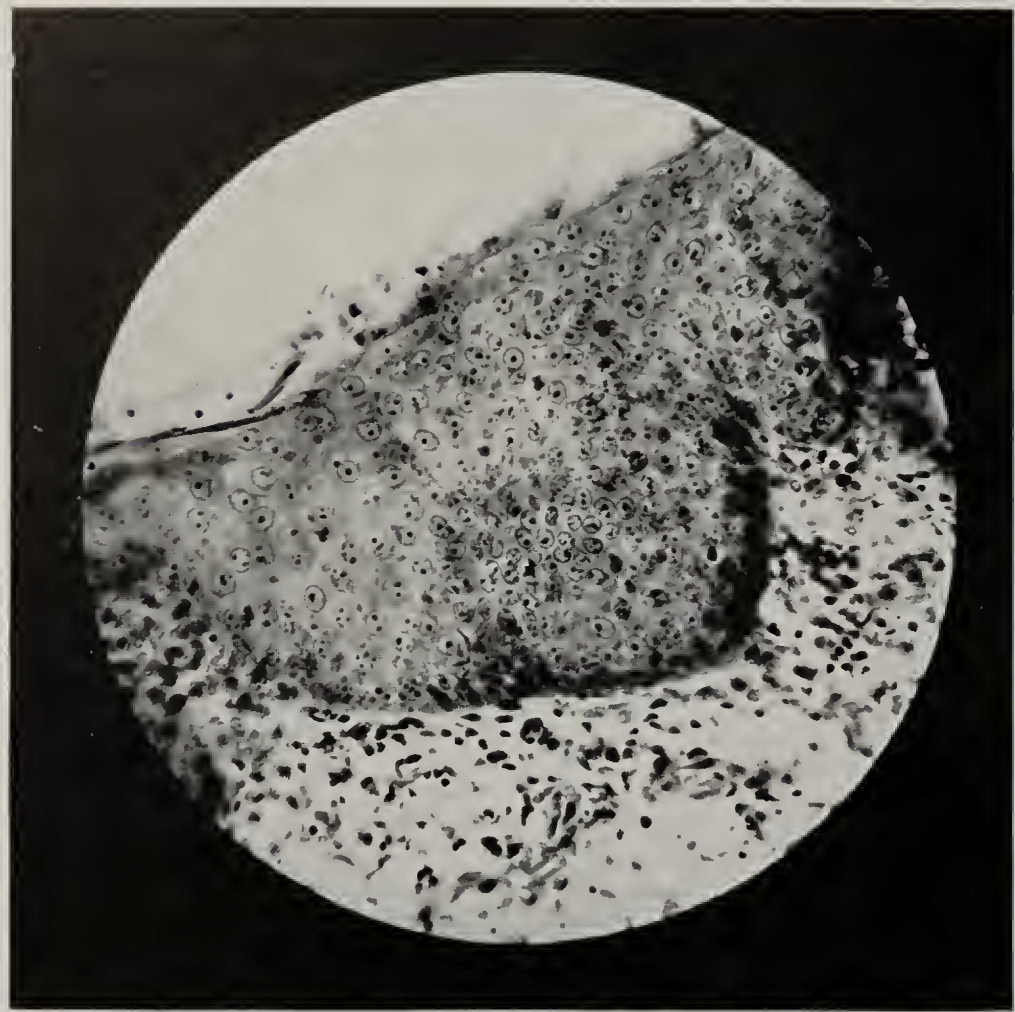

Fig. 12.—19th day. Oesophageal mucosa near suture line showing actively regenerating epithelium.

Fig. 13.—19th day. Inner edge of anastomosis showing union and progressing epithelialization.

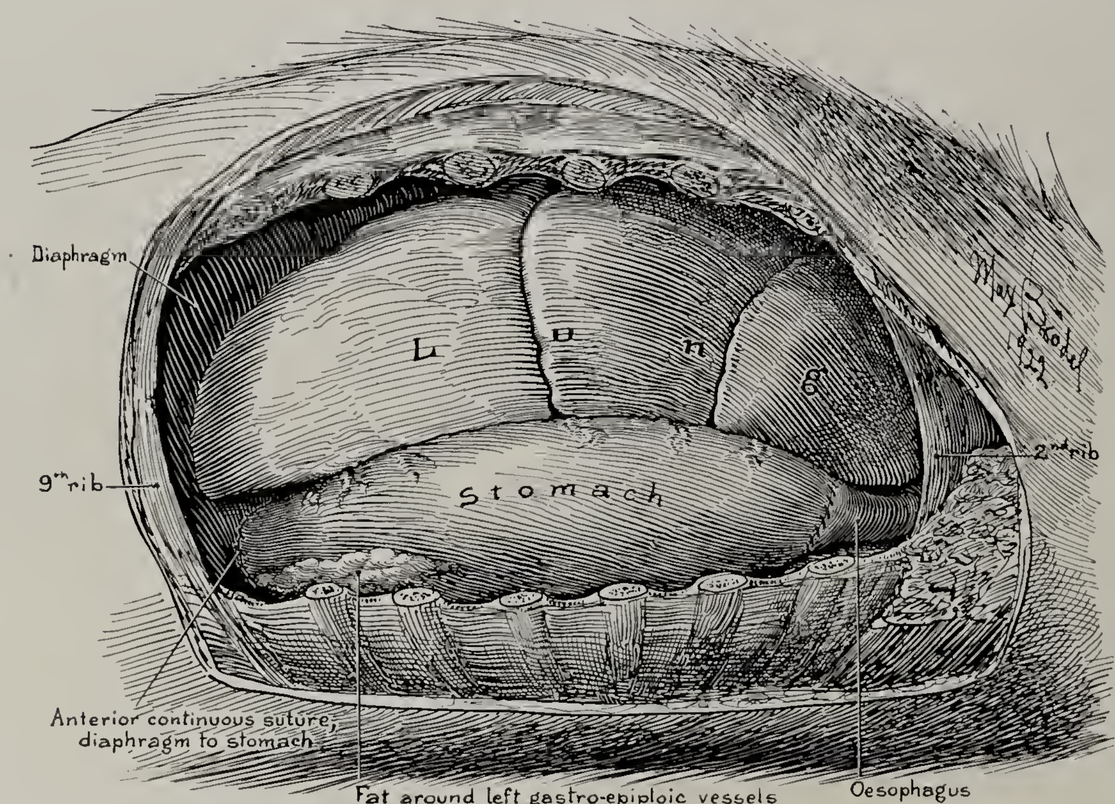

Fig. 14.—Illustrates the possible use of the stomach as a substitute for most of the thoracic oesophagus.

Fig. 15.—Animal killed 48 hours after ligation of phrenic anastomoses in the diaphragm, the coronary artery, the vasa brevia, and the left gastro-epiploic. Stomach viewed from the mucosal surface. Note area of gangrene in fundus of stomach.

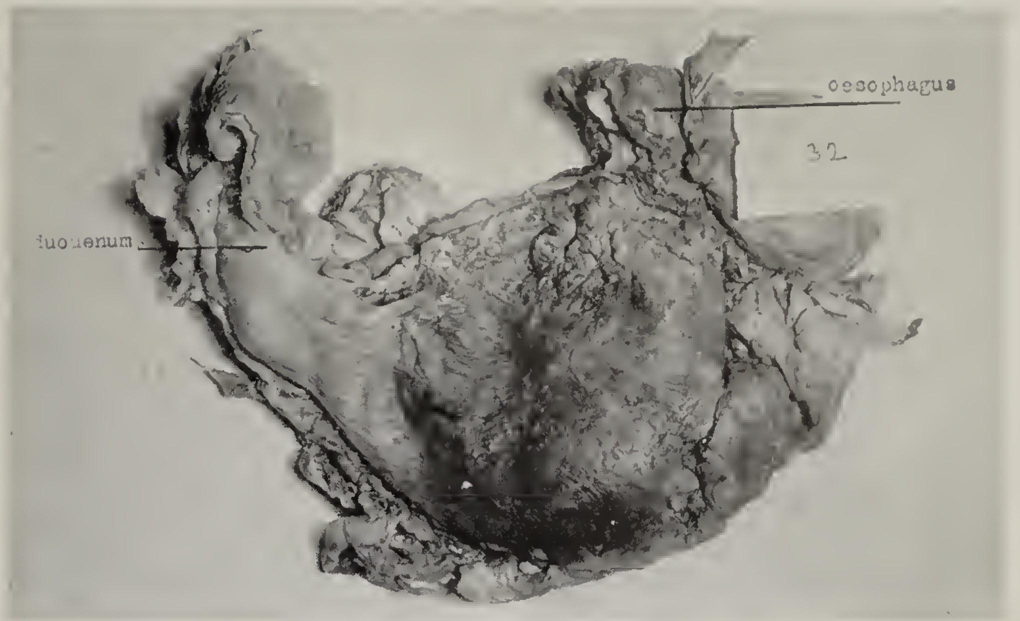

Fig. 16.—Animal sacrificed at the end of 72 hours after ligation of the phrenic anastomoses in the diaphragm, the coronary artery, the vasa brevia, and the left gastro-epiploic. Stomach viewed from the peritoneal surface. Note extensive area of gangrene in the fundus anterior wall.

Fig. 17.—Animal dead 24 hours after ligation of the phrenic anastomoses in the diaphragm, the coronary artery, the vasa brevia, and the left gastro-epiploic. Stomach viewed from the mucosal surface. Note extensive area of gangrene in fundus of stomach.

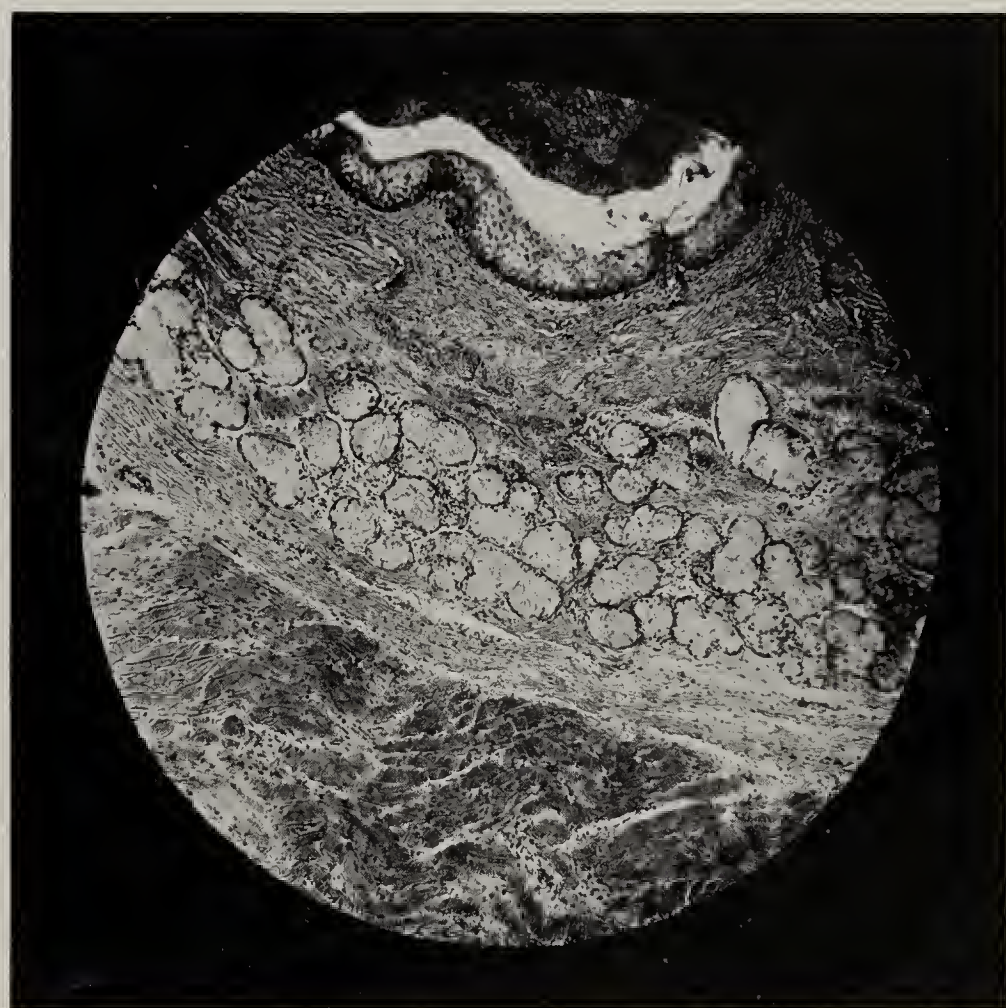

Fig. 18.—Submucosa of the dog's oesophagus. Hemotoxylin-eosin stain.

Fig. 19.—Submucosa of dog's oesophagus. Weigert elastic tissue stain, showing almost entire absence of elastic tissue.

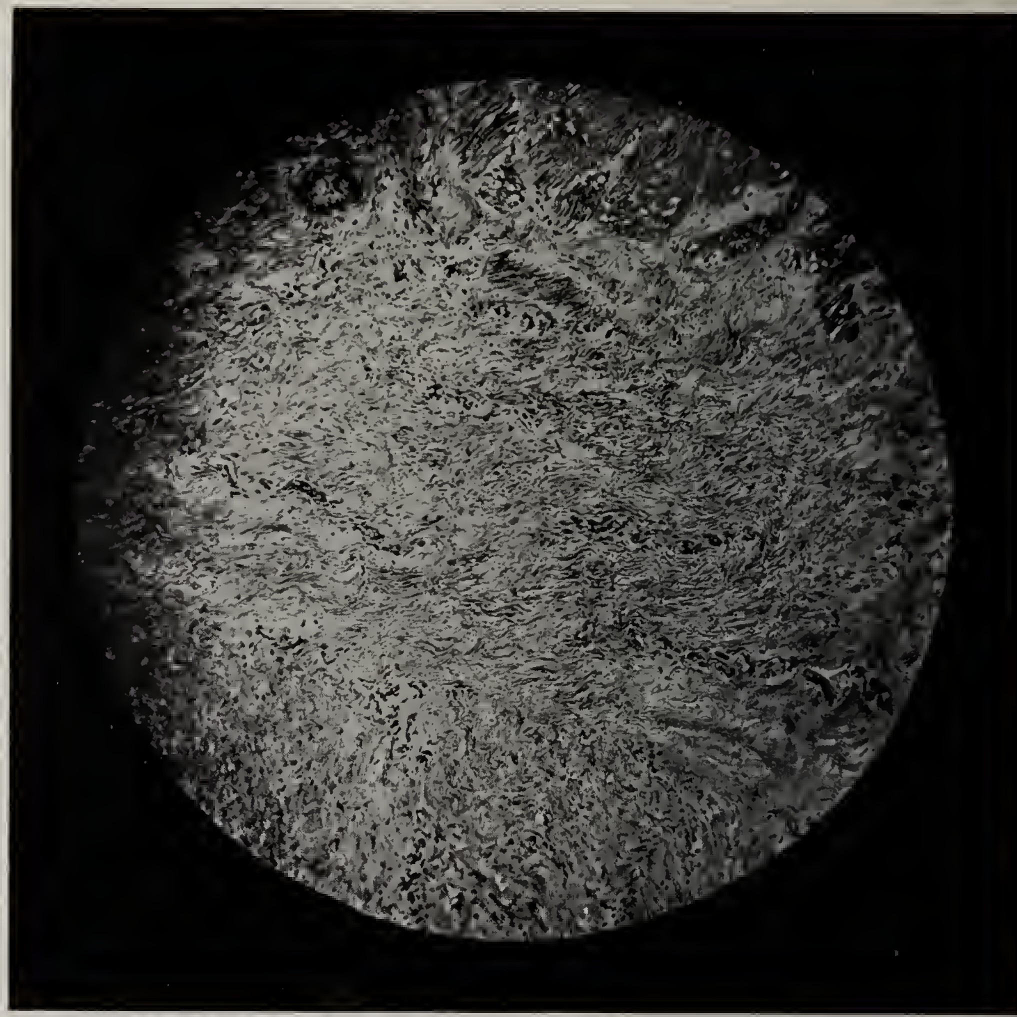

Fig. 20.—Submucosa of the human oesophagus. Hemotoxylin-eosin stain showing muscularis mucosae above and circular muscle layer below.

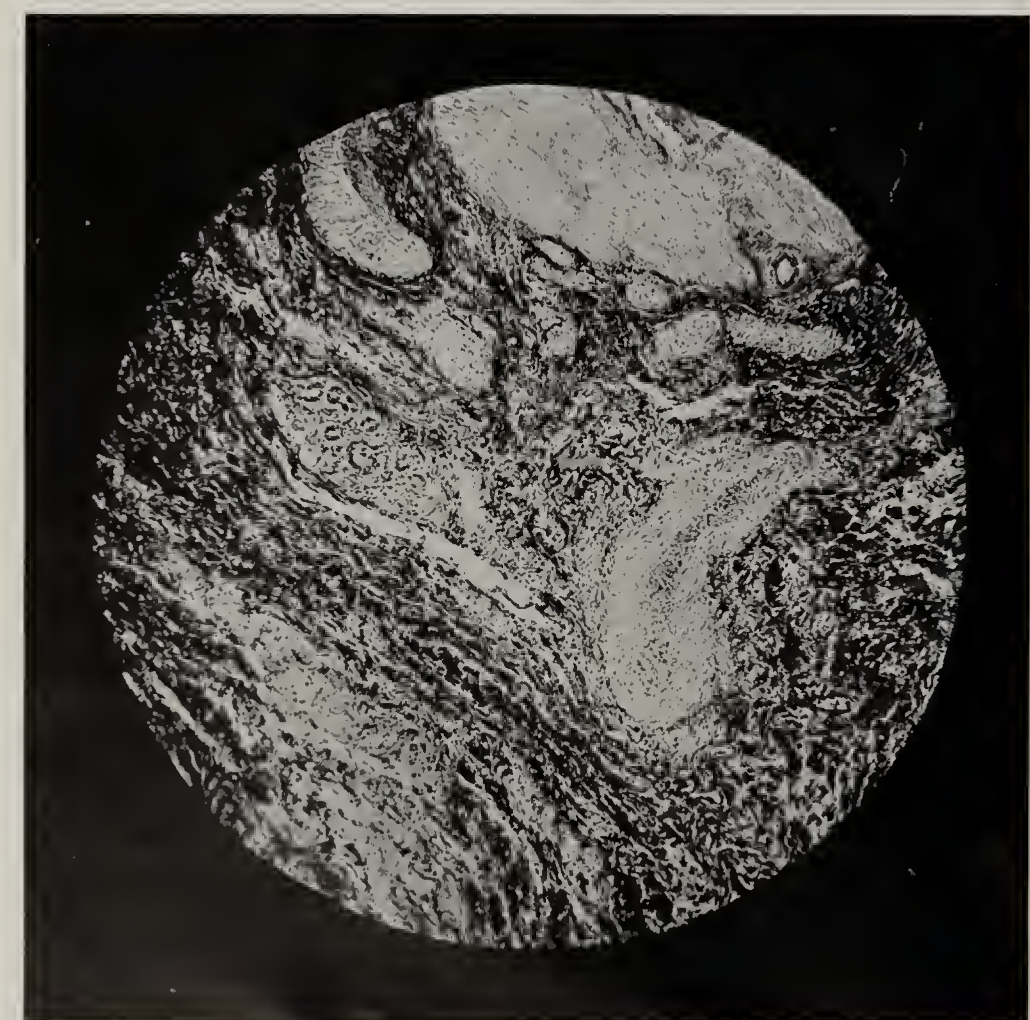

Fig. 21.—Human oesophagus. Van Gieson connective tissue stain, showing well developed submucosa.

Fig. 22.—Submucosa of human oesophagus. Weigert elastic tissue stain, showing relatively large amount of elastic tissue present.

lation of the human stomach may be destroyed without effect upon its viability, W. Braun's [13] statement that four-fifths of the circulation may be so sacrificed, and the expression of an opinion from Alberts [14] that one may ligate widely along both curvatures in man without serious effect upon the stomach. Four experiences with the proposed scheme are reported by Kirschner, but his argument is not entirely convincing. The experimental work we present seems to show clearly that the stomach will tolerate destruction of its circulation up to a definite limit, but that the radical proposal of Kirschner exceeds this limit so far that one would hesitate before adopting it. We feel, however, that division of the three arteries as proposed above is feasible and that if, after division of these arteries, one exercises care to suture the diaphragm to the pylorus or antrum so as to avoid compression of both gastro-epiploic arteries, the chance of necrosis of the stomach wall is exceedingly slight. Mobilization of the stomach after this fashion provides a means for replacing most of the thoracic œsophagus in a dog, but it is only too obvious that the stomach of a healthy dog and the atrophied human stomach below an œsophageal cancer are not entirely analogous; the applicability of the method to man has yet to be demonstrated, but we are very hopeful that it will prove serviceable in resections of the lower third at least.

The Structure of the Œsophagus

Reference has been made above to frequent expression in the literature of the idea that the human œsophagus lacks a well developed submucosa and so offers great difficulty for suture. Successful suture of the gastro-intestinal tract is after all dependent largely upon the tough submucous layer which the stitch grasps and holds firmly. If this tissue is available there is little question of the suture holding. A rather well developed submucosa is readily demonstrable in the human œsophagus, particularly in its lower third.

Histological study of several corresponding levels of the human œsophagus and that of the dog brings out the following points. When the difference in body size is considered, the canine œsophagus is slightly thicker, relatively, than the human, but this added thickness is due chiefly to the bulky longitudinal muscle layer which in the dog is largely of the striated type. Both have a very definite and well developed submucosa of about equal thickness but of decidedly different makeup. In the dog (Fig. 18) this layer consists of areolar connective tissue, the fibres of which are somewhat larger than those of the human œsophagus, but elastic fibres, as brought out by the Weigert method, are almost entirely lacking (Fig. 19). Buried in the submucosa and extending in a complete ring around the dog's œsophagus from the retropharyngeal region to the cardia are numerous mucous glands. The human œsophagus (Figs. 20 and 21) has a submucosa made up of areolar tissue whose fibres are slightly smaller, as a rule, than those of the dog, but elastic fibres are numerous throughout its entire length (Fig. 22), being about as plentiful here as in the submucosa of the stomach or intestine. A few glands are to be found just below the pharynx and again just above the diaphragm, but elsewhere they are infrequent. The muscular layers of the human œsophagus are made up almost entirely of smooth muscle excepting for the presence of a small amount of the striated type in the longitudinal layer for a short distance below the pharynx; in the dog the entire muscular coat is of the striated type in approximately the upper third, below which level the circular layer begins to show smooth muscle, the longitudinal layer remaining almost completely of the striated type throughout its entire length. Histological study thus shows clearly that the human œsophagus has a well developed submucosa and its appearance suggests that this layer offers as firm a grasp for a stitch as that of the dog.

Gross demonstration of the strength of the human submucosa is readily made and seems quite convincing when one considers the following facts. If one strips from a fresh lower third of the human œsophagus its mucosal and muscular layers, there remains a tough tube composed almost exclusively of submucosa. This layer holds the point of a fine intestinal needle so securely that pressure upon its shank will break the needle before the point tears out, a method of demonstration used long ago by Halsted in his work upon intestinal suture. If a freshly removed lower third of the human œsophagus is first divided and then stitched together with two layers of fine silk sutures grasping the submucosa, the first layer consisting of mattress stitches, the second of a continuous stitch, it is found that this suture line withstands the pressure of a six foot column of water without the escape either of fluid or of gas; surely no operation would make such a demand upon the security of a stitch.

It is, of course, obvious that a serosal covering such as the dog has in the lower third is a distinct advantage for the surgeon, and it is probably true that with our present methods there would be a higher incidence of successful suture in such an œsophagus than in one lacking the serosa as the human does, but it is hardly reasonable to abandon our efforts to develop a reliable method of stitching because of this anatomical lack in man. This seems particularly true in view of the histological facts presented above; one may well hope that refined methods of suture will overcome this handicap in human surgery.

Summary

The work here reported demonstrates (a) the feasibility of suture of the œsophagus in the dog, (b) a fairly satisfactory substitute for at least the lower two-thirds of the tube, and (c) the presence of a well developed sub-

mucosa in the human œsophagus. With these facts at hand it would seem that efforts to develop the obvious surgical possibilities are to be encouraged and that persistence may well be rewarded by success in the management of cancer of the human œsophagus. One must keep in mind the fact that, after all, the healthy dog is far better operative material than the diseased human and that, for this reason, sound judgment exercises considerable hesitation before submitting the conclusions of experimental surgery to the test of human application; however, even from a conservative point of view, it would appear that resection and suture *in situ* of the human œsophagus are not beyond the bounds of possibility, but rather offer us definite grounds for hope. The futility of our present management of cancer of the thoracic œsophagus surely justifies us in undertaking procedures of promise even though they involve a greater risk than one would assume willingly. Mobilization of the œsophagus with efforts to construct an extrathoracic tube presents many difficulties, so many, in fact, as to cast grave doubt upon its real usefulness. Lilienthal's [15] case emphasizes the possibilities of extrapleural attack upon cancer of the œsophagus, but this plan of action has definite limitations. The manifold advantages of an adequate transpleural intrathoracic method giving reasonable freedom of action, if such can be developed to the point of practical use, are so evident that persistent effort in this direction seems more than justified; it is in this spirit that our work is reported.

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CLOSURE OF GRANULATING WOUNDS WITH REVERDIN-HALSTED GRAFTS

By Karl Schlaepfer, M. D.

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A skin defect following an aseptic operation is generally repaired by turning in a skin flap from the adjacent region, one of the well-known methods of mobilization being chosen, such a procedure rendering it possible to avoid putting the edges of the wound under too great tension. Wolfe grafts are very seldom used, preference being given, wherever the mobilization method is found unsuitable, to the Ollier-Thiersch grafts. This technic has been employed with great success at the end of the Halsted operation for cancer of the breast; when, instead of putting the borders of the skin defect under extreme tension by attempting primary union, and thereby risking sloughing of the edges with secondary infection and regional lymphangitis, the defect is covered with large Thiersch grafts. By means of this modification *elephantiasis chirurgica**—a chronic lymphangitis in the axilla of the operated side characterized by an intermittent, œdematous swelling of the arm, can be avoided, and perfect function of the arm obtained within a shorter time than with other methods and in every case without difficulty.

Following an accident an extensive lacerated wound may result, with subsequent necrosis of a large area in the soft tissues. In such conditions, owing to the more

* First described by the late Professor Halsted.

marked vascular disturbance in the tissues in the presence of suppuration, infection interferes with the healing and prolongs the illness. In dealing with such a wound, when primary closure is thought unwise on account of the extensive crushing, with vascular disturbance (thrombosis) and subsequent swelling, if the Carrel-Dakin treatment is started immediately after the primary débridement, secondary closure may later become possible. In cases in which the Dakin treatment has not been started until signs of infection have appeared in the wound, or not until later, in the granulating stage, secondary closure is generally impossible because of scar infiltration at the base of the resulting defect. This same condition causes also inelasticity in the neighboring tissue. The grooves resulting after sequestrotomy in cases of chronic osteomyelitis, especially of the long bones, often form chronic sinuses, which resist any attempt at closure. The fact that the tissue surrounding such a wound is immunized by the secretions renders possible the use of pedunculated flaps of muscle, or of muscle, fat, and skin. However, even when these flaps are successfully turned into the defect, they may gape later as a result of the edematous swelling which occurs in the flap as a reaction to the traumatism of the operation and to the simultaneous opening up of so many lymphatics. A secondary dislocation of the flap is a frequent complication following these plastic operations. A fistulous tract as the final result presents a new problem. Healing has not taken place. Moreover, if nails have been used at the time the flap was turned into the granulating groove,—a method for fixation of the flap advocated by many authors—a new focus of osteomyelitis is formed, which endangers the result in still another way. Even when primary closure of the defect has apparently followed the operation, abscess formation with a secondary fistula may result even after months. Filling the cavity with clotted blood and closing the skin over it is a procedure which has been followed by a high percentage of failures. The presence of a latent infection in these wounds endangers the success of any kind of plastic operation. Other difficult conditions which every physician meets are the chronic ulcer of trophic origin, or the X-ray burn. A study of the records of such cases brings out the fact that for them the usual procedures have not proven efficacious.

When confronted by a wound in the granulating stage, a smear must be made in order to demonstrate the bacteriological condition. If numerous micro-organisms are found, the Carrel-Dakin treatment must be started in order to prepare the wound for a method introduced in 1869 by the Swiss surgeon Reverdin. His first experiences were obtained by implanting on leg ulcers small skin grafts composed of all the layers of the epidermis and a small portion of the derma. The skin over the anterior tibial spine having been put on the stretch, a small double-edged knife with a sharp point was introduced into it and after cutting for three millimetres was brought out again. A number of small grafts (measuring 3 mm. in diameter) obtained in this way were distributed all over the defect, 0.5 cm. apart, and the wound was covered with diachylon ointment on linen. The changes in the transplanted grafts noted by Reverdin are very interesting, and have been confirmed by analogous clinical observations in this service. In twenty-four hours after operation the grafts are adherent to the surface of the wound. The individual graft is pale, thickened, and slightly wrinkled. After 48 hours there appears around the graft a grayish area which turns dark red on the third or fourth day. When exposed to the air this zone takes on a dull appearance, like that of cuticle, the surrounding granulation-tissue retaining its glistening appearance because of its moisture. This dry area represents the new epithelium. At this stage the graft is depressed below the level of the neighboring tissue. The new epithelium becomes gray; a new red zone arises outside of this area, and the covering of the defect advances gradually in every direction from the graft.

Reverdin found that each graft possesses a certain chemotactic influence which is active within a certain zone. This zone is the space within which the new epithelium is found to be much more resistant to any mechanical trauma than skin that has grown over from the borders of the defect. Reverdin tested this point in chronic ulcers covered with epithelium in these two different ways. The ultimate fate of the grafts differed; either they remained about the same, being like white islands, depressed or prominent, or they were reduced in size by an exquisite process of desquamation. Sometimes the grafts were lifted up by a profuse secretion, and necrosis resulted. But even in these cases it was noted that a grayish-white island of epithelium appeared after a certain time at some of the places at which the grafts were applied. Certain cell groups of the stratum malpighii remained alive, and grew in their new place. On these experiences is based the principle of the epithelial seed of von Mangoldt, which was rendered practical later by Braun and Pels-Leusden (Reschke) in the form of injections of epithelial suspensions into the granulating area.

It may be of interest to give here a short account of the routine sterilization employed in this clinic for cases in which this method of grafting is decided upon. Two sorts of wounds must be differentiated; deep wounds with several pockets, and shallow or surface wounds, showing only a slight depression compared with the level of the neighboring skin.

The preliminary Carrel-Dakin treatment used in the ulcerated areas to be covered by the modified Reverdin technic is different from the one originally described by Carrel and Dehelly in their paper entitled "Treatment of

infected wounds." In their article will be found the method of preparation of the solution, together with an accurate description of the way in which it is titrated for its sodium hypochlorite content (0.45 per cent)—an important test, to be repeated periodically to insure the efficiency of the method. Its alkalinity (which is essential) is endangered if the solution is not kept in the dark and in a cool place. Neglect of these precautions, which occurs too often, must be held responsible in many instances for the failure of the treatment. The strength of the solution diminishes very rapidly with exposure to light and heat.

In every case a smear must be made from the wound in order to determine its bacteriological condition. The aim of sterilization in deep wounds is to transform the multilocular into a unilocular cavity lined with healthy granulations. The skin around the defect is disinfected with benzine, ether, and alcohol. Gauze sponges are used to swab the wound clean of secretion lying in the depths or in pockets. Irrigation of the wound with Dakin's solution is very helpful. The skin around the defect is covered with vaselinized gauze (squares 3 to 6 inches in size, sterilized in vaseline), great care being taken to bring the squares of gauze into snug contact all along the borders of the defect. A sufficient number of rubber tubes with an opening in the end, combined with others having the openings on the side and the end closed with a silk ligature (see Carrel-Dehelly), are introduced into the wound, to fill all the pockets of the cavity (Fig. 1). They are made to project in groups out of the dressing at different angles, varying with the shape of the wound. The perforated part of each tube must be well inside the wound; the non-perforated, or, as Carrel calls it, the conductive part, comes well outside the dressing (Fig. 2). Loose absorbent gauze fills the space in the opening of the wound and forms the first layer of the dressing. Cotton pads containing on the side toward the wound a thicker layer of absorbent cotton wool, and on the outer side a layer of non-absorbent cotton, both wrapped in a covering of gauze, complete the bandage. Openings are often cut in the pads for the egress of the rubber tubes. Adhesive linen tapes hold the pads in position. The non-absorbent outer layer in the pads, which are kept in stock in one or two sizes, serves to regulate the evaporation of the Dakin's solution from the dressing, and at the same time prevents soiling of the bedclothes.

Irrigation of the wound through these tubes is carried out every two hours during the day and every four hours during the night with a Chetwood syringe (Fig. 1). To each patient is assigned his own bottle of solution and his own syringe. The amount of solution used depends on the number of tubes introduced (one quarter, one half, or a whole syringeful for each tube). After the irrigation is finished the tubes are closed with automatic clips, which prevent any backflow of the liquid. These are temporarily relaxed at each new instillation. With this arrangement the amount of solution carried in through each tube is constant, so that the irrigation of the wound is uniform. In the interval between the irrigations the fluid diffuses somewhat into the dressings and evaporates. After two hours fresh active solution is carried to the surface of the wound. The whole dressing must be changed once a day. After thorough cleansing of the wound and the neighboring skin, the tubes are replaced by other sterile ones. Vaselinized gauze applied snugly to the borders of the defect protects the skin from the macerating effect of constant wetting with the Dakin's solution. In exceptional cases, when the tubes go down into very deep pockets, so that their replacement by new ones would be practically impossible without great traumatism to the tissue and distress for the patient, the tubes are left in, and not until the degree of sterilization of the wound renders it permissible are they replaced by shorter ones, which are changed daily.

Bacterial counts from smears taken from the wound every second day and mapped on a chart supply an accurate record of the degree of sterility obtained. Usually the chart shows a rapidly diminishing number of microorganisms. As soon as several counts show only a few bacteria distributed in numerous visual fields, the sterility is considered sufficient to allow the starting of the transplantation.

In superficial wounds gauze compresses soaked in Dakin's solution are substituted for the Dakin tubes. The preparation of the wound and the neighboring skin is the same as described above. Here also vaselinized gauze must be applied to protect the skin. Cotton pads prevent too rapid evaporation of the fluid. The compresses are changed every two hours during the day and every four hours during the night. A bacterial chart, based on smear counts every second day, gives accurate information of the degree of sterility. In these surface wounds a change of the whole dressing must be made every day.

By using the method of sterilization suited to the configuration of the wound a proper degree of sterility is obtained within a short time. It is then possible to proceed with the transplantation of small grafts, with the technic elaborated in this clinic especially by J. Staige Davis and Mont R. Reid under the guidance and the constant stimulation of Professor Halsted. The grafts are usually taken from the thigh. The patient is given morphine one hour before the operation. The skin area is cleansed thoroughly with green soap and water, followed by benzine, ether, and alcohol, and then painted with tincture of iodine (3.5%). Similarly, but with the omission of the iodine, the neighborhood of the defect may be disinfected. Figure 3 shows the manner of draping the field. The skin from which the grafts are to be taken is anesthetized with procain (0.5 per cent). For nervous adults and for children the administration of gas

during the injection is found to be very helpful (anoci-association). By adding 5 to 6 drops of epinephrin (1:1000) to 3 ounces of the solution the effect of the anesthesia is prolonged without interfering with the taking of the grafts. The injections are made in such a way that depôts of the anesthetic are established outside the zone used for the grafts (blocking anesthesia). In addition, some of the solution is put underneath the graft-area over the fascia in order to block the sensory branches passing through the muscle.

Straight, pointed needles are seized in Halsted clamps (Fig. 3). The iodine over the graft-area is swabbed off with alcohol. The needle is inserted obliquely into the skin, and the latter is lifted up to form a cone, which is then cut with a knife held parallel to the surrounding skin surface (Fig. 3). The graft contains in the center the superficial layer of the corium. It is thicker than the original Reverdin graft, but this additional thickness has been found not to interfere with its growth in the wound. Moreover, it makes the new scar more elastic and more freely movable over the underlying tissue, and thus diminishes its liability to injury. If there is any blood on its inner surface, the graft is dried on a sponge before it is placed in the wound. Still fixed on the tip of the needle, the graft is put into the wound and the curled edges are straightened out very carefully (Fig. 4). A second needle is found of great help in performing this manœuvre. In order to secure a good result, it is important to have the inner surface of the graft brought into perfect contact with the wound. The grafts have also to be cut evenly all through, to avoid the formation of too thick a center. Before the needle is used for cutting a new graft it is passed through the flame of a spirit lamp, to insure absolute sterility. In cutting the grafts one should leave a small area of intact skin (Fig. 3) between each resulting wound. This guarantees epithelization of the defect under the first vaselinized gauze bandage within from 8 to 10 days. The grafts are usually placed 0.5 cm. from each other (Fig. 4), but where sterilization has not progressed uniformly, even a greater distance might be found advantageous. When two men are doing the grafting, the rack devised by Staige Davis is very useful to hold the grafts put on it by one man, ready to be taken up and placed in position by his colleague.

When the whole area has been grafted as outlined above, the wound is exposed to the air for eight hours. A pasteboard box with holes in the sides, or a flexible wire splint (Smythe) cut to the size needed and bent so that it can be held firmly to the skin, forms a good protective apparatus. After eight hours zinc oxide ointment is applied to the skin around the grafted area. One layer of gauze is put over the wound and over the zinc oxide; the ointment keeps the gauze in position, and the gauze fixes the grafts to their base. Salt compresses are now applied over the grafted area, to be changed every two hours during the day and every four hours during the night. After from 12 to 24 hours these compresses are used alternately with Dakin sponges; on the second day the Dakin compresses are used constantly at regular intervals. The less sterile the wound, the earlier the Dakin treatment is started. If after the first 24 hours there is a considerable accumulation of secretion between the threads of the gauze, it is changed; otherwise it is allowed to remain for 48 hours. Later on the whole dressing is changed every day, the zinc oxide also being renewed. On the third day the gauze covering can be left off without danger of displacement of the grafts when the compresses are changed. Instead of zinc oxide for the protection of the neighboring skin, vaselinized gauze may be used in the same way as before the transplantation.

The Dakin compresses can be kept up all the time, the solution serving also to prevent exuberant granulations. If after 10 days to 2 weeks the secretion in the wound is minimal, the Dakin compresses may be replaced by vaseline, applied in a thin layer on sterile linen, or by diachylon ointment. Reid used rubber "protective." Davis shortened the time of healing by using at this stage scarlet red ointment (8 per cent). It is dangerous to stop the use of the Dakin solution too soon; only by its antiseptic power is the infection in the wound kept under control. If replaced too early by the ointments, a flareup of a latent infection may complicate the closure of the defects between the grafts. Exuberant granulations may necessitate a repetition of the Dakin's solution. Only in neglected cases will it become necessary to cut off these granulations and treat them with the silver nitrate stick. Vaselinized gauze dressing for one day, followed by continuous Dakin's compresses, will finally bring about a good result.

The changes observed in the transplants in this clinic are as follows: After 24 hours the grafts, which in the beginning are pale, take on a bluish tinge, or they may remain whitish. This cyanosis increases for 48 hours, after which a reddish point appears in the center of the graft, becoming larger and larger centrifugally and forming an area of new vascularization from vessels growing in from the base. About the third day there appears around the graft a red area, which is somewhat translucent, and takes on a dull appearance when exposed to the air, in contrast with the neighboring glossy granulation tissue. This area, which is new epithelium, increases gradually in size. The graft itself does not change very much in size or appearance, except that it becomes flatter. The new epithelium grows rather fast, suggesting that the different grafts exert a chemotaxis on each other. The granulating area between these islands of epithelium becomes smaller and smaller, so that after 2 or 3 weeks the defect is covered with epithelium.

The epithelium obtained from these grafts and from the outgrowth from them is characterized by its resistance to mechanical injuries, by its particularly rich vascularization, and by its relative elasticity, which is more marked when the thicker Reverdin-Halsted grafts are employed. The elasticity is demonstrated also by the fact that the grooves following sequestrotomy in chronic osteomyelitis become smaller within a few months when grafted in this way. Mont R. Reid and W. F. Rienhoff followed up these cases. By casts taken at intervals they proved that the defect was filling in under the new skin. Although this filling in is partly due to new bone formation as a result of a chronic periostitis, it is also caused by the interposition of new fibrous tissue beneath the new epithelium. In scars obtained by this method of grafting it is interesting to note the way in which the defect is gradually raised to the level of the surrounding sound tissue. The excellent vascular supply of these new skin areas accounts for the fact, observed early by Reverdin, that trophic ulcers are more likely to occur in the skin which has grown in from the borders of the defect than in that which has grown in the grafted zone. As a consequence of the relatively greater elasticity, the secondary retraction of such a scar is also much less.

For this grafting, skin is taken from the patient (autoplasty). Attempts were made to use skin taken from a relative, such as the mother, but they were futile. Even after months, when all the clinical signs pointed to success, the grafts became suddenly necrotic, the condition being associated with signs of a general toxemia. It is possible that biochemistry may demonstrate the existence of skin groups, as well as blood groups, and thus enable us to employ heteroplasty with success (Davis).

Summary.

Every infected wound not suitable for secondary closure can be successfully covered with a very resistant, elastic skin by means of the Reverdin-Halsted transplantation. A thorough preliminary treatment with Dakin's solution, persisted in until relative sterility is obtained, is followed by grafting with small, deep grafts. This method is the technic of choice in treating defects following extensive laceration of the soft parts with secondary necrosis and suppuration, the grooves resulting from sequestrotomy for chronic osteomyelitis, and some cases with granulating areas following unsuccessful plastic operation for empyema. This method has also proved efficacious in the treatment of X-ray burns and of trophic non-specific ulcers of long standing which have proven refractory to all other measures.

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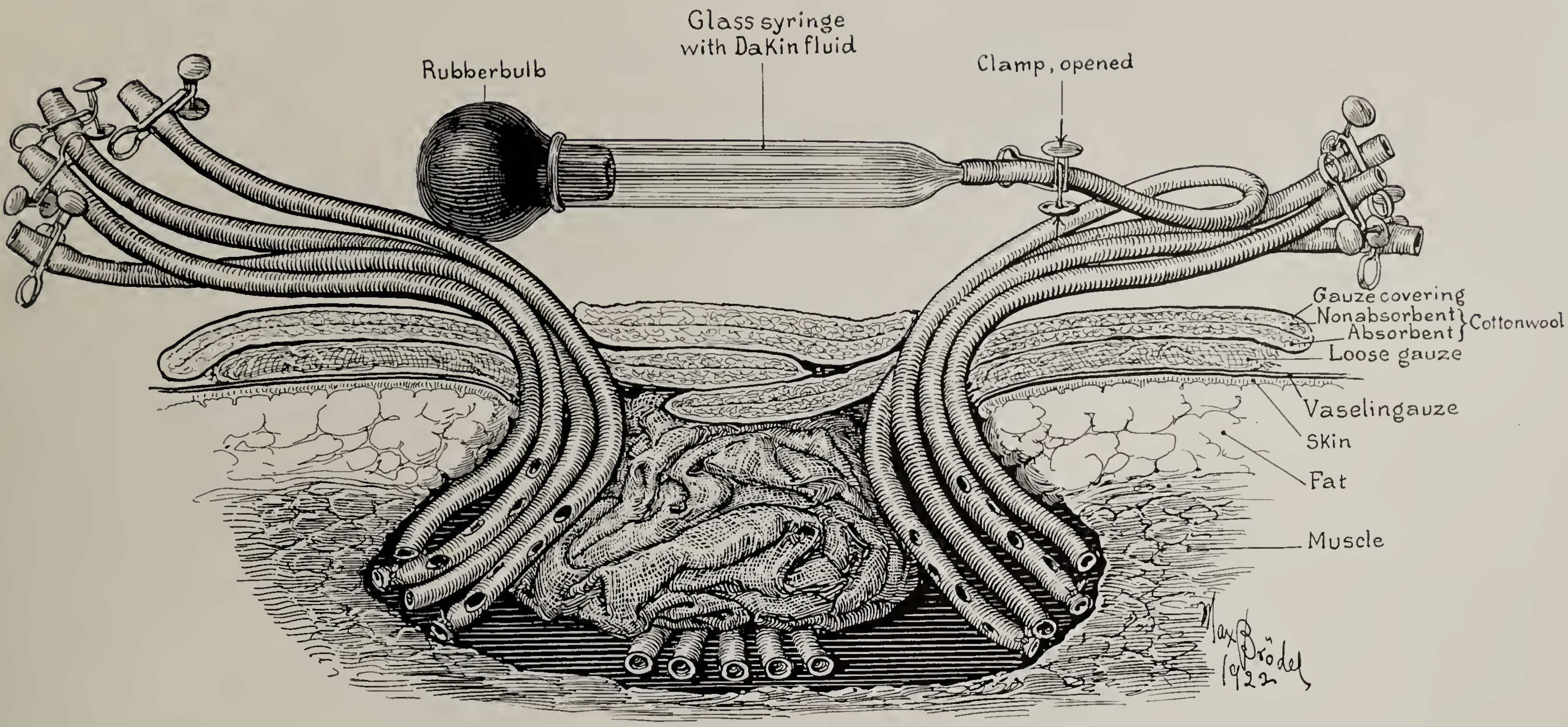

Glass syringe
with DaKin fluid
Rubberbulb
Clamp, opened
Gauze covering
Nonabsorbent
Absorbent
Cottonwool
Loose gauze
Vaselingauze
SKin
Fat
Muscle
Max Brödel
1922

Fig. 1.

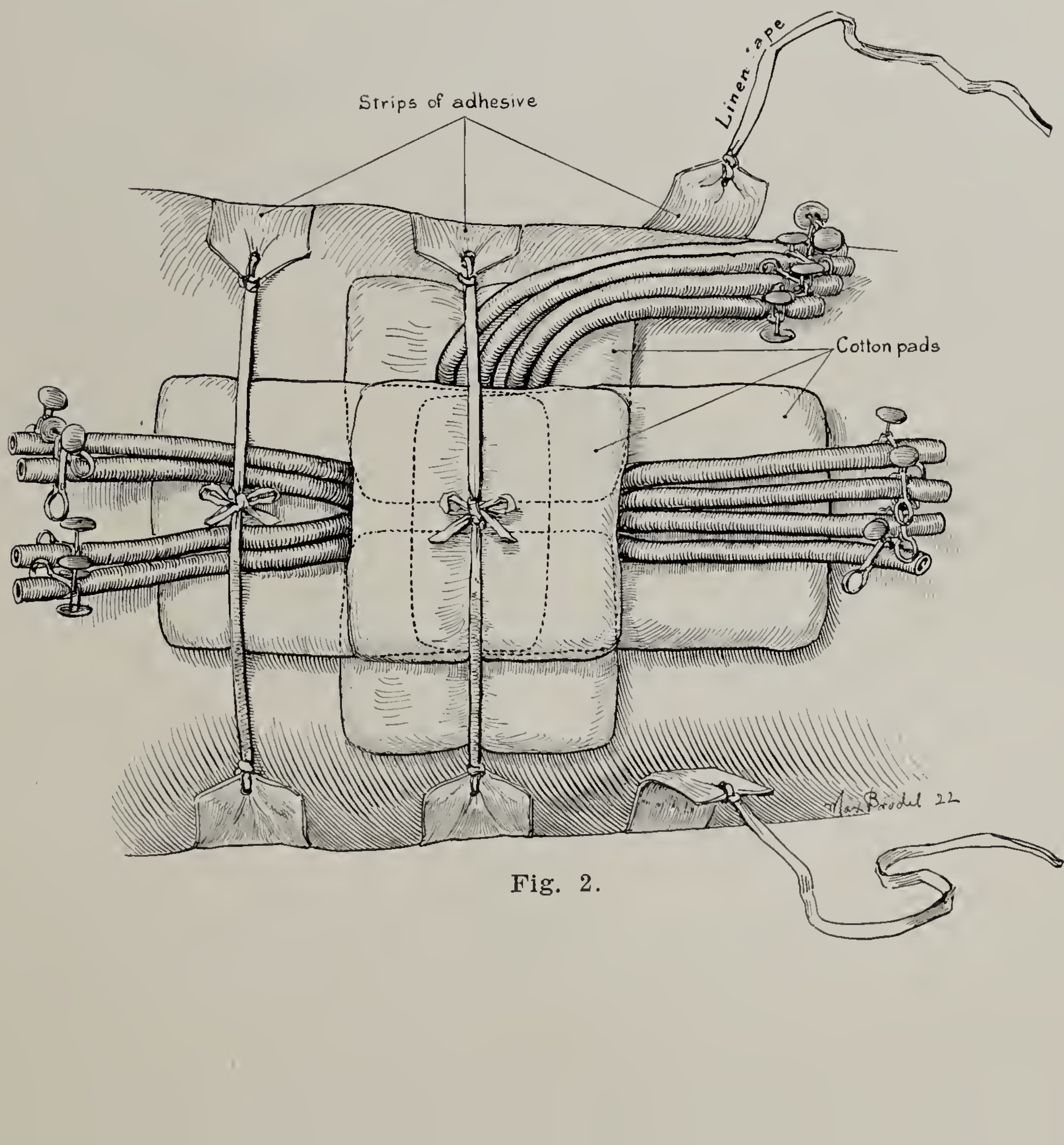

Strips of adhesive
Linen tape
Cotton pads
Max Brödel 22

Fig. 2.

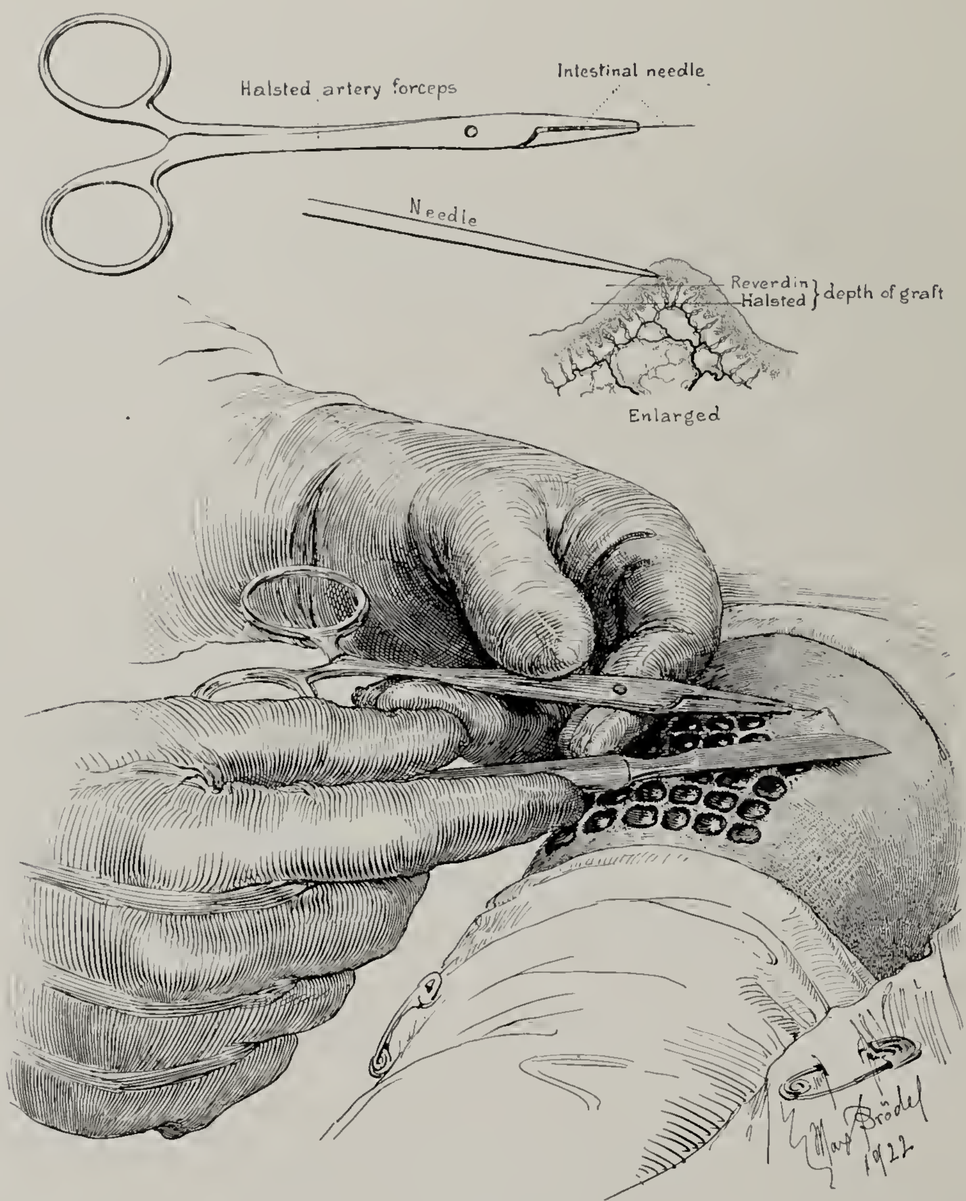

Halsted artery forceps
Intestinal needle
Needle
Reverdin
Halsted
depth of graft
Enlarged
Max Brödel
1922

Fig. 3.

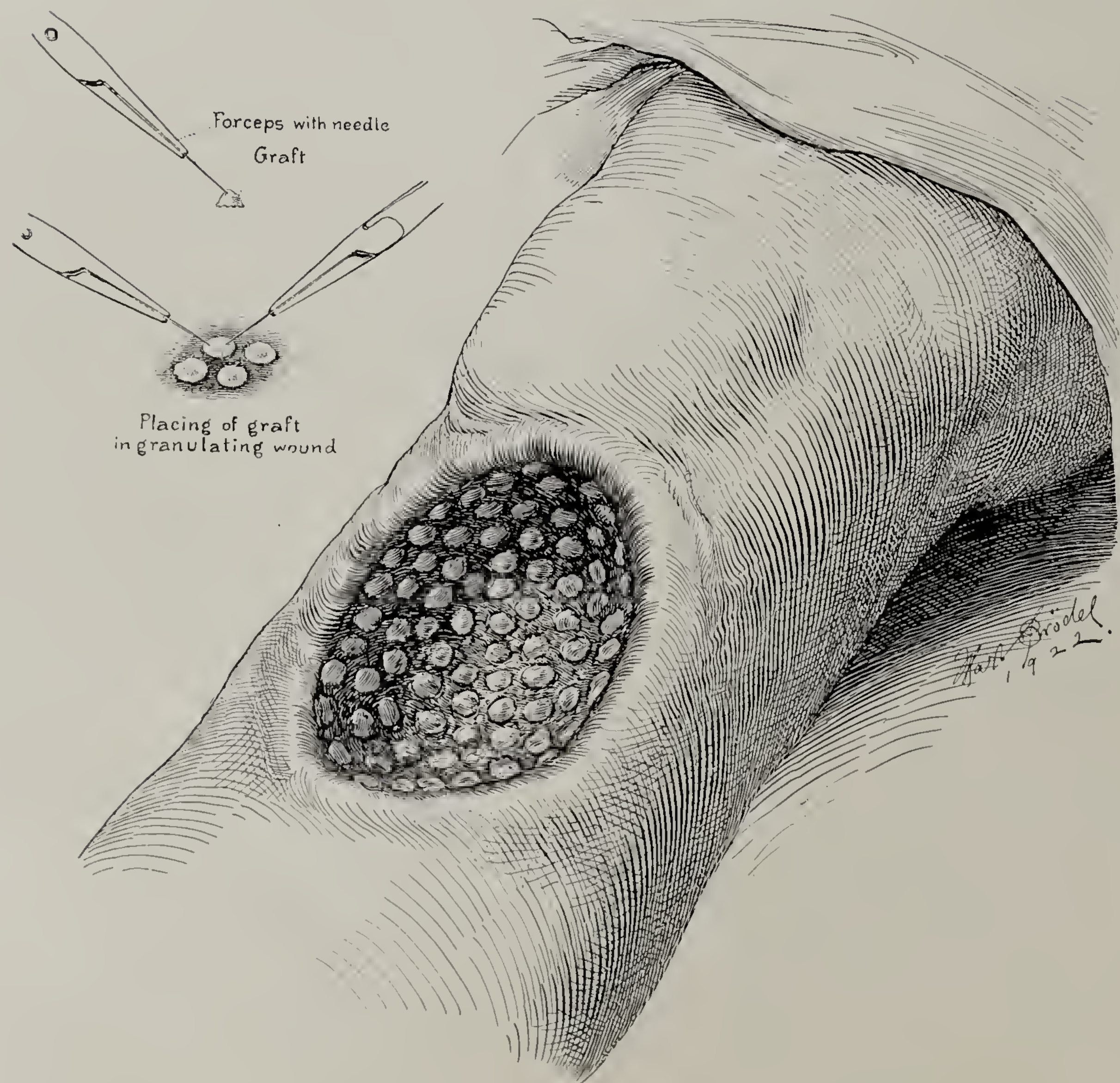

Forceps with needle
Graft
Placing of graft
in granulating wound

Fig. 4.

OBSERVATIONS ON THE TOTAL LUNG VOLUME AND BLOOD FLOW FOLLOWING PNEUMECTOMY

By W. D. W. Andrus, Cincinnati, Ohio

In some previous work upon respiratory physiology in dogs following the removal of one lung,[1] it was found that very definite changes take place in the alveolar air and blood gases. For about thirty days after operation there is a temporary increase in the alveolar carbon dioxide, a fall in the alveolar oxygen, a slight increase in the carbon dioxide of the blood, and a marked decrease in the blood oxygen. By way of compensating for these changes until the enlargement of the remaining lung[2] shall have taken place the number of red blood cells, the hemoglobin and, consequently, the oxygen-carrying capacity of the blood are increased. It seemed probable that in association with these compensatory changes of a respiratory nature there might be other analogous changes of a circulatory nature; and it is with these changes in the circulation in the remaining lung and with the functional enlargement of this lung that this paper deals.

In six dogs (a) the total volume of air in the lungs at the height of inspiration, (b) the amount of blood flowing through the lungs per minute and (c) the pulse rate were determined immediately before operation and immediately after operation, on the first, third and fifth days thereafter and then at intervals of a few days to a week for varying periods up to fifty-seven days.

The total volume of air in the lungs was determined after the method of Van Slyke and Binger,[3] the animal rebreathing from a bag containing 1000 c.c. of hydrogen plus an adequate supply of oxygen until an equilibrium was established between the gases in the bag and the alveolar air. Samples from the bag were then analyzed for nitrogen and hydrogen in a Haldane apparatus to which was attached a colloidal palladium burette for the absorption of hydrogen. The total volume of air in the lungs X was then calculated from the equation:

$$X = 1000 \times \frac{\%\text{Nitrogen}}{\%\text{Hydrogen}} \times \frac{1}{79.2}$$

in which %Nitrogen and %Hydrogen are the percentages of these two gases in the bag at the end of the experiment. The rebreathing was started at the end of quiet inspiration and thus this method gives the sum of the tidal, supplemental and residual air.

For the determination of the amount of blood flowing through the lungs per minute some modification of the oxygen absorption method as used by Plesch,[4] Zuntz[5] Loewy and von Schrötter,[6] and others was considered. However, the oxygen absorption method was discarded because previous work[1] had shown that the oxygen carrying capacity per unit volume of blood is markedly affected by pneumectomy and would obviously impair its accuracy. We have, therefore, used a method by which this value can be calculated from the total minute output of carbon dioxide and the difference in the carbon dioxide content of the arterial and venous blood. To determine the carbon dioxide output per minute the animal was allowed to breathe through an air-tight mask attached to a three-way valve by which the air expired could be collected in a spirometer over water covered with a layer of oil, to prevent absorption of the carbon dioxide. A sample from the spirometer was then analyzed in a Haldane apparatus for carbon dioxide and the total carbon dioxide in the spirometer calculated. Blood samples were then taken, with the usual precautions to prevent contact with air, from the right femoral artery and from the right heart. The blood from the right heart was obtained by inserting a long needle in the fourth right interspace close to the sternum and directing it slightly upward and inward. Determinations of the carbon dioxide content were then made on the whole blood, the apparatus and technic of Van Slyke[7] being employed, and the minute blood flow through the lungs in hundred c.c. "Y" calculated from the equation:

$$Y = \frac{M}{V\text{-}A}$$

in which M is the minute carbon dioxide output and V and A the carbon dioxide content in volumes per cent of the venous and arterial blood, respectively.

Care was taken to have the animals absolutely quiet for some minutes before samples were taken and throughout the experiment. The pulse rate represented the average of several counts with the dog at rest.

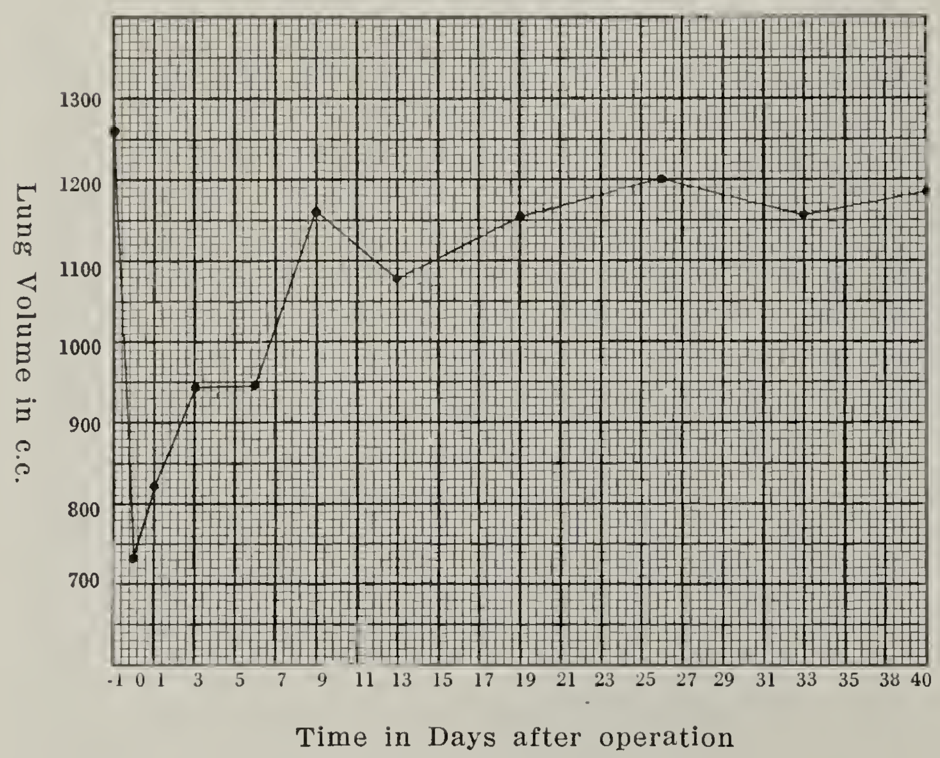
Effect on the Total Lung Volume

Measurements of the total lung volume made within a few hours after operation show an average decrease of about forty-two per cent of the volume before operation. The volume begins to increase at once, however, and in twenty-four hours has risen, on the average, about eight per cent. This rise continues, varying somewhat in amount in the different animals, but showing the same general upward trend in all and reaches about the pre-operative level by from twenty to twenty-six days after operation. It was interesting to note that in one dog that developed distemper seven days after operation the lung volume dropped about forty per cent of its value at that time, owing, we think, to consolidation and therefore "func-

tional removal" of areas in the remaining lung. As the dog recovered, however, the total lung volume increased and reached the pre-operative value by twenty days after operation (Curve 1).

CURVE I.

Lung Volume—Composite Curve

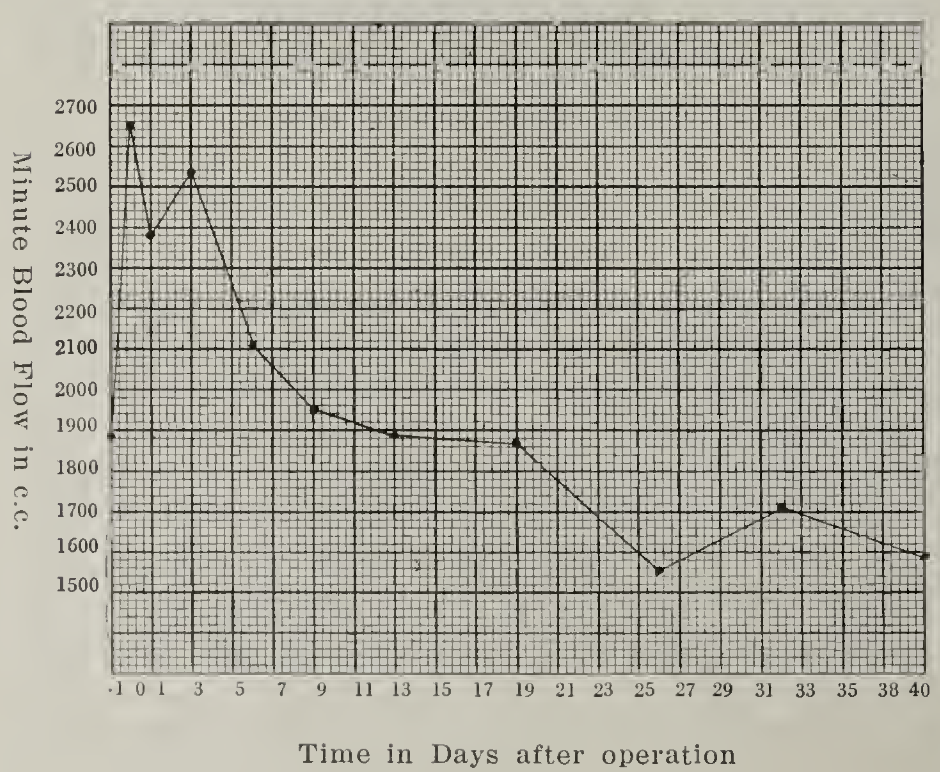


Effect on Minute Blood Flow Through the Lungs

Within a few hours after operation observations show that the amount of blood flowing through the remaining lung per minute is greater than the total amount which flowed through both lungs before operation. The increase varies in the different dogs from 17.2 to 59.1 per cent, the average being 40 per cent. This increase is only temporary, however, the minute flow beginning to decrease in from one to three days after operation, until by about the tenth day it is at about the preoperative level, *i.e.,* the amount which flowed through both lungs before operation. From the twentieth to the fortieth days, in two animals, there was a fall in the minute flow below the preoperative value, but by the fifty-seventh day it had returned to that value (Curve 2). In the dog mentioned above which had distemper there was a secondary rise in the minute blood flow corresponding to the fall in lung volume. The control animals, when subjected to operations other than pneumectomy, showed no such rise in the flow.

CURVE II.

Minute Blood Flow—Composite Curve

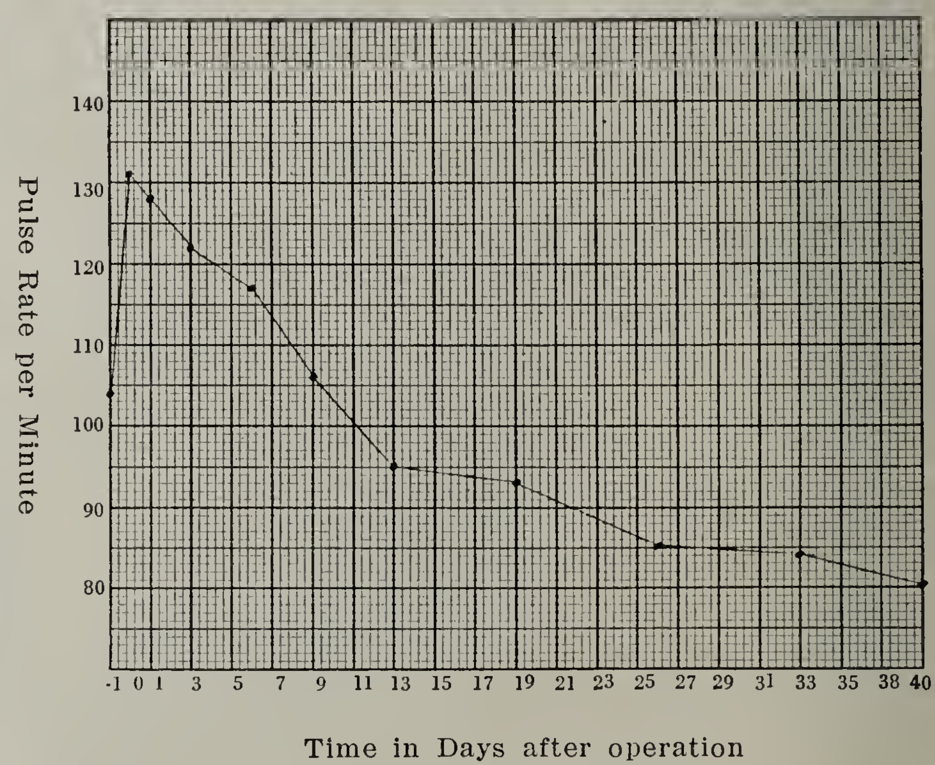


Effect on the Pulse Rate and Pulse Volume

The removal of one lung causes an increase in the pulse rate as observed within six hours after operation which averaged 26 per cent in the six animals, while the controls failed to show any such increase. This increased rate is not maintained, however, for the pulse rate begins to fall within twenty-four hours and reaches the preoperative rate by about the tenth day. The fall continues even beyond this, the pulse rate averaging on the thirtieth day about fifteen beats below the preoperative rate (Curve 3). The increased blood flow runs about parallel with the increased pulse rate, but the secondary fall in the pulse rate is somewhat greater than the decreased flow would indicate and observations on the pulse volume—obtained by dividing the minute flow by the pulse rate—show that about five weeks after operation there is an increase in the output per beat averaging 11 per cent.

CURVE III.

Pulse Rate—Composite. (5 Dogs)



In some unpublished work Heuer has in several instances found a hypertrophy of the right ventricle following pneumectomy and this seems the more interesting in view of the increased pulse volume observed in the animals of this series.

Dog	Days after Operation	Lung Volume in c.c.	Minute Blood Flow through Lungs in c.c.	Pulse Rate
T_{13}	—1	1367	1869	96
	0	803	2196	120
	1	938	2294	130
	3	1030	2655	124
	6	1091	2114	108
	9	1160	1920	96
	13	1209	2045	94
	19	1290	1862	80
	26	1440	1500	84
	34	1310	1700	80
	41	1350	1575	80
	65	1300	1900	96
T_{14}	—1	1040	1456	108
	0	730	1920	132
	1	802	2104	144
	3	1030	2298	120
	7	940	1984	120
	13	562(D)	2309(D)	128(D)
	19	1008(D)	1585(D)	90
	26	967	1510	90
	33	993	1520	90
	40	1017	1395	90
	49	1100	1550	94

Dog	Days after Operation	Lung Volume in c.c.	Minute Blood Flow through Lungs in c.c.	Pulse Rate
T_{16}	—1	1010	1710	96
	0	619	2055	132
	1	638	1989	120
	5	900	1978	128
	7	720	1858	120
	12	940	1680	100
	19	1018	1860	96
T_{17}	—1	1420	1850	120
	0	763	2944	150
	1	861	2260	138
	3	850	2055	138
	5	926	1930	120
T_{18}	—1	1260	1860	96
	0	725	2180	116
	1	850	2080	108
	3	890	2076	108
	5	990	2050	108
	10	1100	1750	102
	17	1200	1850	100
T_{19}	—1	1470	2530	110
	0	900	2800	120
	1	975	3100	136
	3	1300	2550	112
	5	1100	2667	116
	12	1260	2210	102

SUMMARY

In addition to the previously observed effects of pneumectomy in dogs the following changes of a respiratory and circulatory nature have been observed:

(a) A marked decrease in the total lung volume which persists for about thirty days, then returns to normal.

(b) A transient increase in the pulse rate and the blood flow through the remaining lung persisting for about ten days, followed in both by a fall slightly below the preoperative value. The pulse rate falls by a greater amount than does the blood flow through the lung, indicating an increase in output per beat of the right ventricle.

The decrease in lung volume is to be considered a detrimental effect of pneumectomy; while the increase in blood flow and pulse volume may be taken as compensatory mechanisms.

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CHANGES IN THE FALLOPIAN TUBE DURING THE OVULATION CYCLE AND EARLY PREGNANCY

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INTRODUCTION

In view of the extensive cyclic changes of the internal genitalia which have been observed in the human and practically all of the laboratory animals—and which involve even the vaginal mucosa in some species at least, *e.g.* guinea-pig, rat, mouse—the observation of any part of the reproductive tract, such as the Fallopian tubes, promises results of definite interest. The Fallopian tubes of the pig afford special opportunity for observations that are complete for all stages of the reproductive cycle, especially with regard to the changes related to the passage of the ova.

Previous observations on the structure and function of the tubes are of more than historical interest inasmuch as numerous clinical hypotheses relating to tubal pregnancy, placenta praevia, sterility, etc., have been based upon them. The epithelial lining of the tubes has been the center of interest. In 1886, Frommel [5] distinguished in man and some of the lower animals the non-ciliated cells and described their resemblance to secretory epithelium, in contrast to the adjacent ciliated cells. Since then, periodic changes in the structure and function of these elements, chiefly with regard to ciliation, have been described in man, the rabbit, pig, mouse, etc.

Cyclic changes in the distribution of the cilia, with the alternation of a ciliated and non-ciliated (secretory) phase have been described in the human (Tröscher,[13]

Schaffer [12]) and most of the laboratory animals (Moreaux,[10] Katz,[9] Schaffer,[12] Gianelli [6]). These authors hold, in general, that during oestrus and pregnancy, as well as menstruation in the human, the ciliated cells are diminished in number and the non-ciliated cells which appear to be secretory are increased. In the tubes of the mouse, Allen [1] (p. 335) has described cyclic changes in which a loss of cilia from some of the ciliated cells is followed by extrusion of their nuclei into the lumen of the tube, the extrusion of nuclei in the ciliated portion beginning in the early metoestrum and continuing in a marked degree sometimes to the middle of the following pro oestrum.

Such changes have been held to influence the transport of the ova in many animals, as for instance in man, where (as expressed by Grosser,[7]) "the chief driving power in the wandering of the ovum in the uterus as well as in the tube is the ciliary current." For further discussion of the rôle of the cilia and the clinical hypotheses which have followed, reference is given to a previous paper (Corner and Snyder [4]).

In evaluating the preceding observations it is to be borne in mind that, in most species which have been investigated, knowledge of the uterine and ovarian cycles is scarcely adequate for a complete study based on the selection of all stages of the cycle. What is needed is a detailed description of the structure of the Fallopian tube at all stages of the cycle, and the correlation, by all available technical means, of these changes with the known state of the uterus and ovary at parallel stages, in non-pregnant animals and in early pregnancy, to the end that the alterations of structure in the tube may be studied from a broad functional viewpoint; only in this way can such details as ciliary activity, etc., be correctly appreciated.

Method and Material

The present observations mark such an attempt to view the Fallopian tubes of the pig throughout all stages of the reproductive cycle and early pregnancy, and to correlate definitely the condition of the epithelium with the functional state of the ovary, ova, and uterus. The selection of material has been carried out according to the principles followed in a previous study [4] (p. 360) of the uterine ciliation, which for the sake of convenience may be quoted here.

The domestic sow was chosen on account of the abundance of material available, and also because of the fact that recent work on the reproductive cycle of this species makes it possible to select from the uteri obtained at the abattoir a series which shall be representative of all stages of this cycle, and to study these in the light of the ova and embryos in this species.

The choice of material representative of the successive stages in the 21-day cycle of the sow was made, upon the basis of previous acquaintance with the events of the cycle, by inspection of the ovaries and by search of the Fallopian tubes and uteri for ova, and was confirmed by microscopic study of sections of the corpora lutea and the uterine mucosa. The necessary data have been given in a monograph by Corner (1921) and need only brief mention here.

Thus, during the three days following ovulation there are freshly ruptured follicles (i. e. early corpora lutea) in the ovaries, and the ova may be recovered from the Fallopian tubes. About the fourth day the ova pass into the uterus, whence they may be recovered by washing out the uterine canal. By the seventh day the corpora lutea are solid, and have reached a diameter of 9 mm. The microscopic picture is now that of full maturity. About the seventh or eighth day the ova disappear by degeneration within the uterine cavity, and thus the second week is characterized by the presence of fully matured corpora lutea in conjunction with the absence of ova from the tube and uterus. About the end of the second week the corpora lutea suddenly degenerate, as indicated by a beginning diminution in their size, by an increase in the firmness of their texture, and by a change of color from the fresh color of maturity to a yellowish tone. The microscope reveals degeneration of the granulosa lutein cells. During the latter part of the third week the new crop of Graafian follicles begin to exceed the resting stage of 4 to 5 mm. diameter, until finally they reach the mature diameter, 8 to 10 mm. Their rupture at the end of the third week marks the beginning of a new cycle.

By the aid of these criteria, and by comparison with the characteristic cyclic histologic changes of the uterine mucosa, as illustrated in the above-mentioned monograph, it is possible to assign a given specimen of the internal genitalia of a sow to its correct place in the cycle, within a few days, and thus to collect any desired series of stages directly from abattoir material.

The following list enumerates the specimens upon which the present observations are based, the non-pregnant specimens having been dated by the method given in the quotation above, and the pregnant specimens having been dated by comparison of the contained embryos with the Normentafeln of Keibel:

NON-PREGNANT		PREGNANT	
Day of cycle	Number of Specimens	Day of cycle	Number of Specimens
1st -3rd	6	7-8-9-10th	7
4th-7th	5	14th	1
8th-10th	3	16th	2
10th-15th	4	17th	2
15th-20th	6	18th	1
		21st	1

After observation of the specimen *in vivo,* satisfactory fixation of the epithelium was obtained by allowing the fixing fluid to flow through the lumen of the tube from a small pipette at one end. Bouin's fluid was found to be a satisfactory fixative; a few specimens were fixed in 10 per cent formol. Sections from the ampulla of the tube were stained with iron-hematoxylin, and hematoxylin and eosin. The height of the epithelium was measured with a Zeiss micrometer from tracings obtained by means of a camera lucida and oil-immersion lens.

Observations

A good introduction to our observations may be made by considering the appearance of the tubal epithelium in the living state, as seen in bits of tissue taken soon after

arrival of the fresh specimens at the laboratory, and flattened under a coverslip, as Nylander did in Leydig's [8] laboratory in 1852, when he discovered active cilia in the uterus of the sow. In such preparations taken from the isthmic, ampullar, and fimbriated portions of the tube, active cilia may always be seen at all stages of the cycle, without apparent alteration in distribution or activity. Even under the low powers of the microscope the cilia can be seen beating for several hours at least, without the addition of a nutrient fluid such as Locke's solution or the use of a warm chamber.

Closer study of the epithelial surface of the tube shows that it is composed of ciliated and non-ciliated cells which are about equally distributed. A few small rounded cells are seen at irregular intervals packed in between the cylindrical epithelium, and are found in sections to have deeply staining nuclei. While observing the active cilia at all stages of the cycle, marked changes in the non-ciliated cells become evident even *in vivo*. Thus the appearance and textural conditions of the epithelial surface along the tubes are changed strikingly at different times during the three weeks of the cycle. For instance, in the tubes in which ova are in transit and are recovered in the washings (oestrus or 1-3 days after ovulation, Fig. 1) the surface appears smooth, and the distal ends of the non-ciliated cells lie, in general, at about the level of the basal granules of the ciliated epithelium. On the other hand, during the second week after ovulation (period of implantation and mature corpora lutea, Fig. 2) the surface becomes studded with finger-like cytoplasmic projections from the non-ciliated cells, which extend toward the lumen of the tube two or three times farther than the cilia. These pseudopod-like processes still show a clear-cut rounded outline like a cell boundary, and within them may appear globules of varying refractility, and sometimes nuclei.

In the fixed preparations the changes can be followed in greater detail. The height of the epithelium is found to vary periodically. It is more than twice as high when the ova are passing through the tubes (1-3 days after ovulation, Fig. 1) than during the second week after ovulation (period of implantation, Fig. 2). The maximum height, averaging 25 micra as measured from the basement membrane to the level of the basal granules of the ciliated cells, falls to 10 micra during the second week after ovulation, when the corpora lutea are mature. During the third week (Fig. 3) a rise in the height of the epithelium marks the gradual return to the maximum height characteristic of oestrus and the first few days following ovulation.

This periodic rise and fall in the height of the epithelium of the tubes is made especially conspicuous by the coincident changes in the non-ciliated cells, previously noted in the living tissue. The length of the projections from the non-ciliated cells is found to vary inversely with the height of the epithelium. As the epithelium becomes lower during the second week after ovulation (period of implantation, Fig. 2), striking changes are evident in the non-ciliated cells, as cytoplasmic projections from their distal ends jut out far beyond the adjacent cilia. The deeply staining nuclei may be seen not infrequently extending into such protrusions, which, as they increase in length, tend to become pedunculated and may occasionally break away. As the epithelium increases in height again during the third week after ovulation (Fig. 3), the projections tend to disappear, until at the time of ovulation, and throughout most of the first week afterwards, the distal ends of the non-ciliated cells become flattened out nearly on a level with the basal granules of the ciliated cells and rarely extending to the tips of the cilia.

The nature of these curious cytoplasmic projections which have also been seen in the uterus of several species (see Corner [3]) remains obscure. Staining tests show that they do not contain mucin, nor have any other special histochemical features been noted, other than those of the cytoplasm from which they project. The presence of cilia at all stages of the cycle without apparent variation in number is verified by examination of the fixed material. The nuclei of the ciliated cells often lie closer to the surface of the epithelium than those of the non-ciliated cells, when the epithelium is high during several days preceding ovulation and almost a week following it. Thus the appearance of an outer and inner row of nuclei may often become evident.

In spite of the extensive periodic alterations in the epithelium, signs of regenerative and degenerative processes such as mitotic division, "Stiftchenzellen," or chromatolysis are not prominent at any stage. Rounded cells with deeply staining nuclei and lying near the basal margin of the epithelium are found in small numbers throughout the cycle.

The fluid content of the connective tissue stroma of the tubes appears to be altered periodically. The stroma appears swollen and œdematous when the epithelium is high during the first and third weeks after ovulation, in contrast to the closely packed strands when the epithelium is low, during the second week.

Wandering cells of the eosinophilic and plasma cell types appear in numbers that fluctuate sharply but irregularly without any apparent relation to the cycle. Few neutrophilic leucocytes are seen.

Turning now to our specimens taken from pregnant animals, (Fig. 4) and studying them in the light of the foregoing observations upon the non-pregnant, we note the striking fact that, if pregnancy intervenes, the periodic changes are inhibited. The epithelium of the tube tends to remain in the condition characteristic of the second week after ovulation (when the corpora lutea are mature, Fig. 2). For instance, in a tube from a preg-

nancy of about 18 days (embryos of 23 somites, Fig. 4) the epithelium (9 micra) is not more than half as high as in the non-pregnant animal of the same stage (Fig. 3). Similarly, the cytoplasmic projections from the surface of the non-ciliated cells are more than twice as long in the pregnant as contrasted with the non-pregnant. The connective-tissue strands of the stroma are closely packed. In tubes of about the ninth day of pregnancy (1 mm. blastocysts) at about the time of implantation, a marked infiltration of eosinophilic leucocytes is evident.

No change is observed in the distribution or activity of the cilia in pregnancy.

Discussion

From the foregoing observations it seems evident that in the Fallopian tubes of the pig periodic changes occur in the height of the epithelium, in the surface and morphology of the non-ciliated cells, and in the fluid content of the stroma. These cyclic alternations parallel the corpus luteum rather closely in its three phases: growth (1st week), full development (2nd week), and retrogression (3rd week, Fig. 5). Thus when the ova are passing along the tubes early in the first week after ovulation, the epithelium is of maximum height (25 micra) with the surface of the non-ciliated cells flattened and smooth (Fig. 1). When implantation is occurring in the uterus during the second week the epithelium reaches the minimum height (10 micra), and finger-like cytoplasmic projections jut out from the surface of the non-ciliated cells far beyond the cilia, completely altering the textural conditions along the lumen (Fig. 2). Perhaps these projections represent a response of the tissues derived from the upper portion of the Müllerian duct in the same manner as that which in the uterus facilitates the implantation of the embryos, as Corner [3] has demonstrated. When the new crop of Graafian follicles is rapidly maturing during the third week after ovulation (Fig. 3), the epithelium increases in height and the surface of the non-ciliated cells tends to become flattened to nearly the level of the basal granules of the ciliated cells.

The presence of the fullgrown corpora lutea that mark pregnancy (Fig. 4) is accompanied by an inhibition of the periodic changes in the epithelium and stroma of the tube, and the persistance of the low epithelium and long cytoplasmic projections seen during the second week after ovulation. Curves corresponding to changes in size of the corpus luteum and alterations in the height of the epithelium of the tube are almost parallel (Fig. 5).

No significant alteration in the distribution or activity of the cilia occurs at any time throughout the reproductive cycle or early pregnancy, in the tubes of the pig. No evidence in support of an alternation of a ciliated and non-ciliated (secretory) phase is noted. It is suggested that the strikingly altered surface of the non-ciliated cells, especially during the 2nd week after ovulation, when the corpora lutea are well differentiated, may help explain the previous observations describing a periodic transition from a ciliated to a non-ciliated (secretory) phase. There is no support in these observations for clinical hypotheses regarding tubal pregnancy, sterility, placenta praevia, etc., based upon the influence on the transport of the ova, of the supposed alternation of ciliated and non-ciliated phases in the epithelium of the tube.

Summary

1. There are periodic changes in the Fallopian tubes of the sow, involving the height of the epithelium, the surface and morphology of the non-ciliated cells, and the fluid content of the stroma.

2. The cyclic alternations in the tubes closely parallel the corpus luteum in its phases of growth (1st week), full development (2nd week), and retrogression (3rd week).

3. Pregnancy inhibits the cyclic alternations in the tubes of the sow, and the epithelium tends to remain in the state which is found in the second week after ovulation, when the corpora lutea are full grown.

4. Active cilia are seen at all stages of the cycle without apparent alteration in distribution or activity.

5. These observations give no support for clinical hypotheses explaining pathological conditions of implantation and sterility on the basis of an alternation of ciliated and non-ciliated (secretory) phases in the epithelium of the tubes.

Grateful acknowledgment is due Dr. Corner of the Department of Anatomy for the generous supervision and suggestions which made the work possible.

DESCRIPTION OF PLATE

Fig. 1. Epithelium and stroma of Fallopian tube of the pig during oestrus (ova found in tubes). × 700.

Fig. 2. Tube about 12th day after ovulation. × 700.

Fig. 3. Tube during latter part of 3rd week following ovulation (17th-20th day). × 700.

Fig. 4. Tube during 3rd week of pregnancy. Embryos of 23 somites (17th-18th day) found in uterus. × 700.

Fig. 5. Curve showing height of epithelium of Fallopian tube of the pig at successive stages of the ovulation cycle and early pregnancy, in comparison with Corner's diagram of the ovarian cycle.

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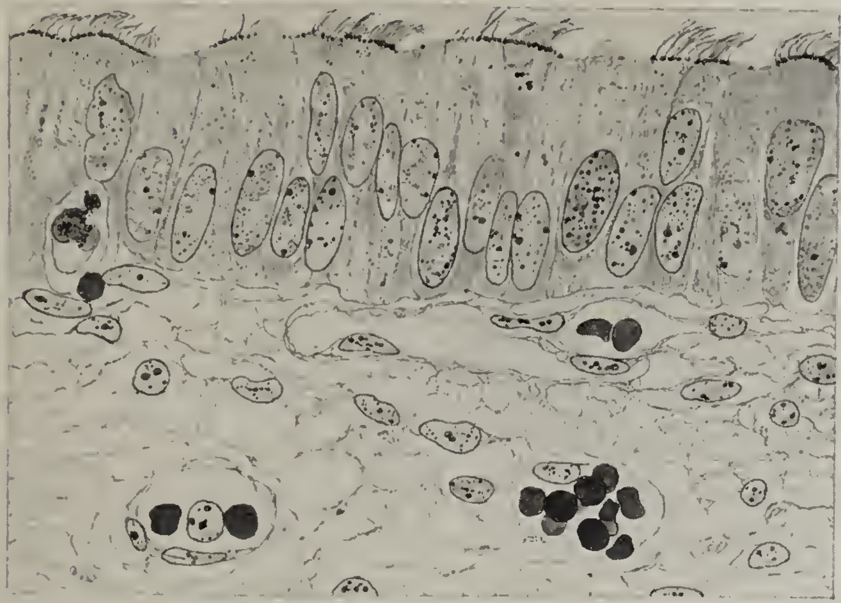

Fig. 1.

Fig. 3.

Fig. 2.

Fig. 4.

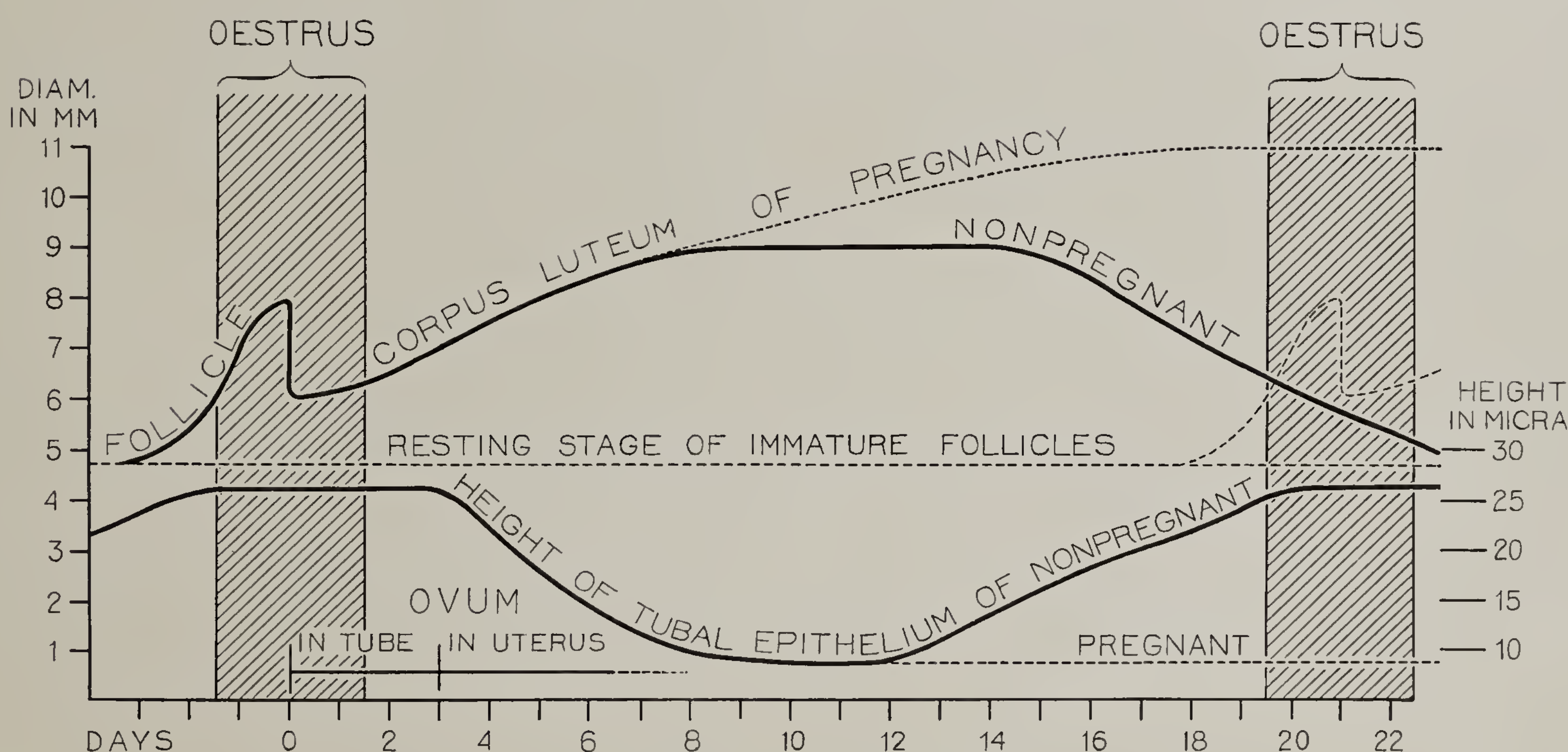

Fig. 5

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AN EXAMINATION OF THE SPINAL ACCESSORY NERVES FROM A CASE OF BILATERAL ACQUIRED SPASMODIC TORTICOLLIS *

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Within the past fifty years the surgical treatment of spasmodic torticollis has been widely practised, but notwithstanding the many opportunities which have thus been offered for the acquisition of anatomical material, there are few recorded instances in which the nerve tissue has been subjected to microscopic examination. The cervical musculature has, however, been the object of searching investigation; and an occasional necropsy has furnished material for pathological study of the brain and spinal cord.

Section of the spinal accessory nerve for the relief of spasmodic torticollis is said to have been first practised by Campbell de Morgan [1] in 1862, although his account of the operation did not appear until four years later. Isidor [2] found, however, that Bujalski, as early as 1843, had divided the individual branches of the nerve as they entered the sternomastoid and trapezius muscles. Nerve stretching was then adopted by Annandale [3] but later on, having found this procedure to be of no benefit, he cut the nerve. Collier's [4] method of ligating the spinal accessory with silver wire at one time was thought to be an effective procedure, but Gould [5] claimed to have secured more lasting relief by avulsion of the central end of the divided nerve. Excision of the nerve was then practised by Rivington, Smith, Southam, Ballance, and other European as well as American surgeons, while later on Keen [6] devised an operation which included division of the posterior rami of the upper four cervical nerves. Isidor's thesis of 1895 contains a critical analysis of all the operations which had been performed up to that time upon the spinal accessory and posterior cervical nerves; but his review and my own search of the subsequent literature upon the surgical treatment of torticollis reveal only one instance in which the excised nerve has been studied microscopically.

So far as I have been able to determine, Southam [7] was the first to examine the resected spinal accessory nerve in spasmodic wry-neck. He found proliferation of the connective tissue and neuroglia and in portions of the section disintegration or total absence of the myelin sheath; so that in these demyelinated areas, "the axis-cylinders were the only remaining normal elements." His laboratory technique is not recorded. Five months previous to the resection, the nerve had been subjected to stretching, and Southam attributes, no doubt correctly, the pathological changes to the result of this earlier operation. Hence the only study, thus far recorded, of the previously uninjured nerve must be accredited to Ballance [8] who, five years later, described a case in which the affection was unilateral and apparently confined to the sternomastoid and trapezius. About one inch of the spinal accessory nerve was resectioned and preserved for further investigation. Without reference to his staining methods he concludes his paper with the following sentence: "The microscopic examination of the excised portion of the nerve did not reveal anything abnormal."

Kader,[9] in an elaborate monograph, for the most part dealing with the congenital form of the disease, apparently confined his anatomical investigation to a study of the muscles. Sections were especially prepared, however, for examination of the intramuscular nerve fibres and in most instances these were of normal appearance, although slight thickenings of the endoneurium and moderate round-cell infiltration were occasionally noted. In some of the sections the nerve fibres were faintly stained and the axis-cylinders terminated abruptly in a cone-shaped process surrounded by clusters of lymphocytes. The motor end-plates were unaltered. Kader apparently did

* Read before the Philadelphia Neurological Society, October 27, 1922.

not examine the nerve trunk and, although he regarded the changes in the intramuscular nerve fibres as secondary to the myositis, it was his opinion that true spasmodic torticollis may be the result of a primary nerve affection.

Thus, in the account of the following case, the pathological examination of the nerves is of particular interest, while the bilateral character of the spasm, with the production of marked retroflexion of the neck, and the history of a preceding infection are the clinical features to which attention is directed.

J. S., a male, aged 19, single, came to the Johns Hopkins Hospital Dispensary (F.94878) on May 19, 1918, complaining of "swelling and stiffness of the neck." Both parents were living; the mother was then healthy; but the father had suffered from headaches and stomach trouble, and one sister had been subject to migraine. In other respects, the family history was without significance.

The patient was a full-term child, delivered without instrumentation, and at birth showed no physical imperfection. With the exception of whooping-cough and measles during childhood, there was no history of illness until 4 years before admission when, at the age of fifteen, he had a "nasty, high fever" of several days' duration. This, according to his mother, left him in a highly nervous condition from which he never fully recovered, notwithstanding the faithful administration of osteopathic therapy for a period of nine months. In 1916 he had a purulent discharge from the right ear. He had worn glasses for a number of years, but had never suffered from diplopia or strabismus. The cardiorespiratory, gastro-intestinal, and renal systems were without evident disease. Venereal infection was denied and a history of secondary manifestations was not obtained. He smoked but did not use alcoholic beverages.

In February, 1918, an abscess of the right thigh confined him to bed for several days and, while suffering from this infection, a drawing sensation accompanied by swelling and stiffness of the muscles was first experienced upon the right side of the neck. The head was then deviated to the left. Within a few days, the muscles upon the left side of the neck were similarly affected and later those at the back of the neck became stiff and swollen, so that the head was now drawn backward. The spasm was said to have become fully developed within a period of ten days or two weeks, and since then there had been only brief intervals in which it was possible to hold the head in the erect posture or to flex it upon the chest. During sleep the contractions ceased and the diminution in the size of the muscles was such that, upon awakening in the morning, he could wear with comfort a "fourteen" collar; whereas by noon the size of the neck had so increased that it was necessary to change to a collar two sizes larger. This nocturnal variation in the symptoms has continued throughout the illness.

Examination revealed a well-nourished and physically well-developed man who did not give the impression of being particularly neurotic. His head was held in almost constant retroflexion, with the chin deviated slightly to the left so that when sitting in front of the patient one looked directly into the nostrils. The swelling and hypertrophy of both sternomastoid muscles were, however, the most striking features (Fig. 1). Occasionally, the retrocollic spasm ceased for a short period during which the chin could be voluntarily flexed upon the thorax; but the head was almost immediately drawn backward by a contraction which began simultaneously in the two trapezii and the posterior muscles on both sides of the neck, and subsequently involved the two sternomastoids. The head was then fixed in the position shown in Fig. 2, with a degree of tonicity which could not be overcome either actively or passively. Although tremor and spasmodic twitching were sometimes noted in the right arm, there was no additional evidence of disease of the nervous system.

Upon further study after admission to the Church Home and Infirmary, May 30, 1918, it was noted that there were many carious teeth, marked pyorrhea, and follicular tonsillitis; but physical examination of the thorax and abdomen disclosed no abnormality, and the urine contained neither albumin nor sugar. Although the erythrocytes were normal in appearance and number, a leucocyte count of 11,840 was recorded. A slight rise of temperature of the septic type was attributed to the oral and pharyngeal infection. The blood Wassermann test was negative, and a radiogram of the cervical spine failed to show any disease of the vertebræ. On twenty successive days measurements of the neck were made in the morning, at noon, and in the evening, and it was noted that the largest measurement, 39 cm., was uniformally obtained at noon. Toward evening the swelling would gradually subside, so that the morning measurement was usually 2 or 2.5 cm. less than that obtained at mid-day.

It seemed desirable to eliminate the obvious foci of infection, and Dr. E. H. Teeter accordingly removed the tonsils and carious teeth. The operation was followed by evident improvement in the patient's general condition. The temperature remained normal, the retrocollic spasm was less intense, and the variations in the size of the neck were not so great. Nevertheless, the muscular spasm persisted to a marked degree and on August 29, 1918, Dr. Teeter sectioned two unidentified posterior cervical nerves, both spinal accessory nerves, and the sternomastoid, the trapezius, the splenius capitis, and the semispinalis on both sides. All of the muscles were greatly hypertrophied and slightly edematous. A portion of each muscle and of each spinal accessory nerve was placed in 10 per cent. formalin for microscopic study.

The anatomical material was cut in cross and longitudinal sections, and the nerve tissue stained with hæmalum and acid fuchsin, phosphotungstic acid, and by the Weigert method, while specimens of the muscles from both sides of the neck were treated with hæmotoxylin and eosin, the Van Gieson stain, and iron-hæmatoxylin.

The Spinal Accessory Nerves.—The left nerve, in cross-section, stained with hæmalum and acid fuchsin shows many faintly colored, swollen axis-cylinders of irregular outline, with only an occasional healthy-looking axone in the entire section. There is no cellular or connective-tissue proliferation, nor is there any evidence of an acute inflammatory reaction. With the nerve cut longitudinally the fragmentation and swelling of the axis-cylinders are more apparent, and there is perhaps slight increase in the neurilemma nuclei. In the phosphotungstic acid preparation (Fig. 3), the neurofibrils appear to be separated into irregular fasciculi occupying most of the myelin space, but examination of the longitudinal section shows that this arrangement is probably due to fragmentation of the axis-cylinders. The Weigert stain reveals a complete absence of myelin. The right spinal accessory nerve presents, by all methods of staining, a more nearly normal appearance, although in the Weigert preparation the myelin takes the stain faintly and, in portions of the section, is completely decolorized.

Fig. 1.—Retrocollic spasm showing swelling and hypertrophy of both sternomastoid muscles. Except during sleep and for brief periods of relaxation, the head occupies this position throughout most of the day.

Fig. 2.—Retrocollic spasm. Lateral view showing degree of retraction of head and hypertrophy of the sternomastoid.

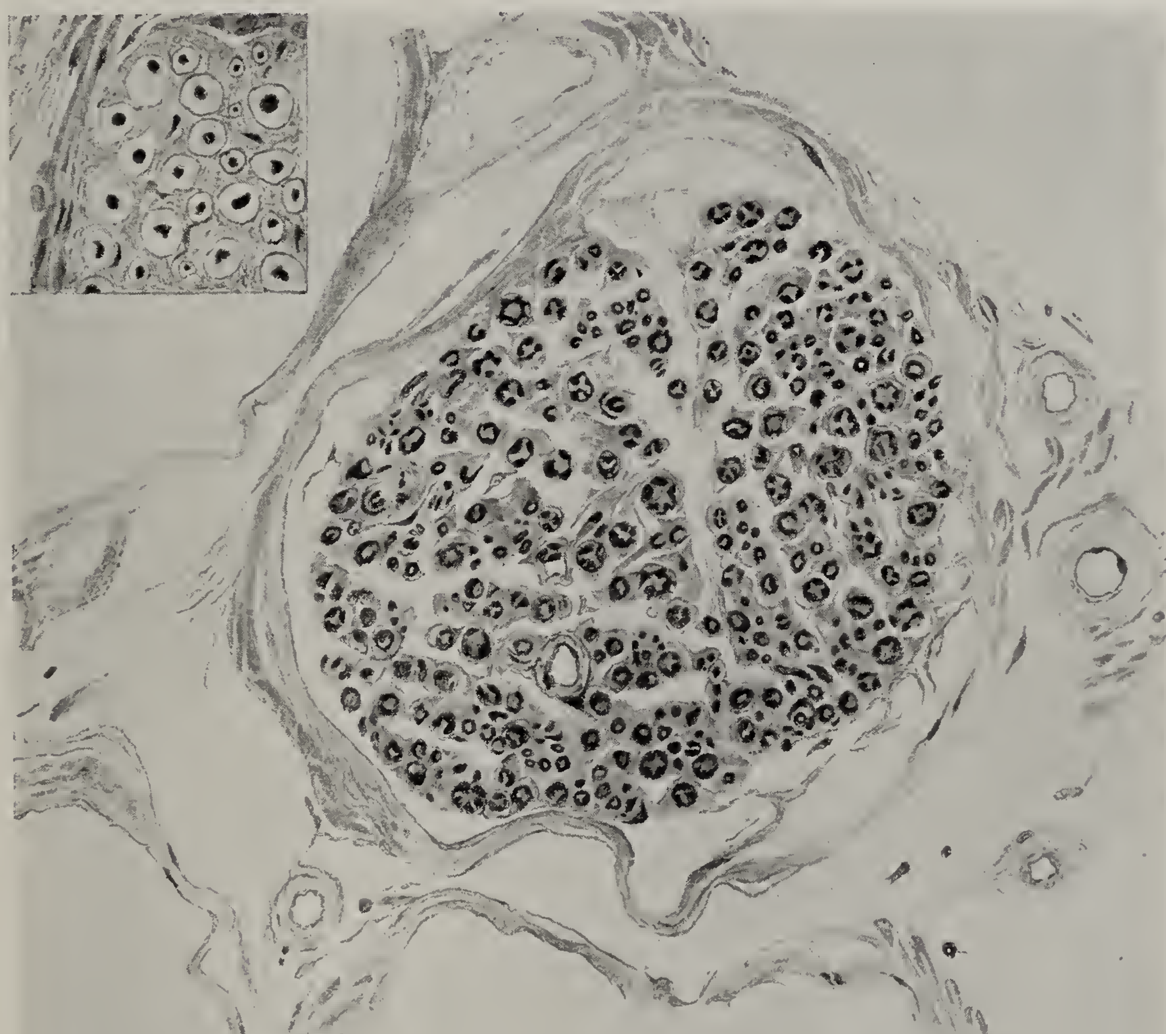

Fig. 3.—Cross-section. Portion of the left spinal accessory nerve. Phosphotungstic acid stain. Camera lucida drawing, Oc. 3, Obj. 6, Leitz, showing disintegration, fragmentation and distortion of the axis-cylinders. The insert in the upper left corner represents a portion of a normal spinal accessory nerve stained by the same method and sketched to the same magnification.

The Muscular Tissue.—In general, all of the specimens exhibit the changes commonly observed by those who have ·eviously studied the muscles in torticollis. Most of the specimens are well stained, but the muscle cells vary in size and shape. Some are round, elliptical, or polygonal and in a process of simple atrophy, while others are greatly hypertrophied and show longitudinal cleavage. The sarcolemma nuclei are not particularly increased and, as a rule, the cross striations are well preserved. A more pronounced lesion is observed in the splenius capitis where, in addition to the changes already noted, many of the muscle cells are dumb-bell in shape, vacuolated, and undergoing general disintegration. The muscles of the left side appear to be more severely affected than those upon the right.

Although it is not uncommon in wry-neck to find a predominant unilateral spasm associated with feeble contraction of some of the muscles of the opposite side, the approximately equal involvement of the two sides is quite unusual; and I have been able to find only two instances of well-marked retrocollic spasm in the literature. Gowers [10] has met with the condition once, and Cassirer [11] has recently described a case, with autopsy, in which retroflexion of the neck was preceded for several years by torsion spasm of the extremities. One of Southam's [12] three cases was of the bilateral type. The congenital disease, although of an entirely different nature, occasionally affects both sides, and Morse [13] has reported a case of this type, with the note that Hildebrand [14] had also recorded a similar observation. Thoms [15] has, however, since reported a third instance of the bilateral affection in infancy.

Of the many causes to which the acquired disease has been attributed, cervical arthritis, trauma, septic intoxication, the infectious diseases, occupation, and psychogenic disturbances are thought to be the more important etiologic factors. It is of interest in connection with the subject of this study that Fitz Simmons [16] finds dental infection a not improbable cause of the disease, and Isidor refers to a case reported by J. Mitchell in which relief followed the extraction of carious teeth. Whether or not the intoxication is productive of a parenchymatous degeneration of the spinal accessory and posterior cervical nerves is not known; and although Ballance has intimated that the affection may be due to irritation of the spinal accessory nerve or its nucleus, the opinion seems to be general that spasmodic torticollis is not dependent upon a disease of the peripheral nerves. It is not improbable, however, that the cervical nerves may be implicated in the bony changes which Marie and Léri [17] have recently described in the cervical vertebræ, nevertheless, it is difficult to understand how a lesion confined to the vertebræ would explain the frequent involvement of the spinal accessory nerve without, at the same time, producing some evidence of spinal cord disease.

That contraction of the cervical muscles may be a symptom of disease of the cortex, the meninges, or the spinal cord will be generally admitted, but the neuropathology of genuine spasmodic torticollis is unknown and unstudied. Those who regard the affection as an organic nervous disease have suggested that it is probably due to excessive motor discharges from the cortical or spinal centers, while Babinski finds, in some cases, clinical evidence of a lesion in the pyramidal tracts. Although I have been unable to secure the original account of the necropsy, it is stated by Marie and Léri that no lesion was found in the central nervous system in the case studied by Dejerine. According to Sicard and Robineau,[18] Tretiakoff attributes the affection to disease of the corpus striatum; while, in a case of torsion spasm associated with wry-neck, Cassirer discovered bilateral degeneration of the caudate and lenticular nuclei. The discovery of this lesion, together with the clinical observation of a patient in whom wry-neck was the initial symptom of a subsequent torsion spasm, suggested to Cassirer the common origin for torticollis, torsion spasm, and dystonia musculorum progressiva. There is not sufficient evidence, however, to accept his conclusion that all spasmodic wry-neck is only an episode in the development of this nuclear syndrome.

There is also some evidence, from a study of lower animals, that a spinal lesion may be the cause of the muscle spasm. Edward Crisp,[19] in 1875, described the occurrence of torticollis in the common fowl. The hen was found with its neck twisted from right to left, while the cervical vertebræ formed nearly a semicircle with the point of the head directed upward. When the hen was placed in a basket and its head secured in the normal posture, the convulsions ceased. Autopsy revealed a "large ecchymosed spot over the second cervical vertebra" and three clots of blood, the size of millet seeds under the outer covering of the cord on the left side.

Since division of the peripheral nerves often fails to secure relief, Meige is of the opinion that, in man, the source of irritation is situated above the spinal center; and that the impulse arising at this higher level is probably transmitted by the vascular sympathetic system. It has also been suggested that the affection may be due to a disturbance of the vestibular or cerebellar function.

With this limited knowledge in the past and my unconfirmed study of today, there is no evidence upon which to formulate any reasonable conception as to the nature or location of the lesion in acquired torticollis; and whatever may be the significance of the changes which have been described in the spinal accessory nerves, we are forced to the conclusion that the neuropathology of spasmodic torticollis is in need of further investigation.

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ON THE EXISTENCE OF MORE THAN FOUR ISOAGGLUTININ GROUPS IN HUMAN BLOOD *

Part III.*

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OUTLINE

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Part III

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Note.—The preceding portions of our report appeared in the issues of this Bulletin for February and March, 1923.

PART III

VIII. The Bearing of These Findings Upon Reactions Following Transfusion

The question naturally arises, what light is shed by these findings upon the unexplained reactions following transfusion? This question we cannot answer completely

* Presented before the Medical Society of the Johns Hopkins Hospital, October 16, 1922.

as yet, but there are some points on which it may be well to comment.

It should be mentioned that, other things being equal, the frequency of recognizable reactions after transfusion varies directly with the care used in looking for them; careful observations and an hourly temperature chart reveal many otherwise overlooked. Dr. Alan Chesney has tabulated the results of transfusions recently performed at this hospital and has kindly placed his data at our disposal (see Table XXV).

TABLE XXV.

Post-Transfusion Reactions

Temperature	All transfusions, all services. Aug. 1, 1921 to June 1, 1922		Transfusions for Pernicious Anæmia. Aug. 1, 1921 to June 1, 1922		Transfusions for Pernicious Anæmia. Aug. 1, 1920 to Aug. 1, 1921	
	No.	Per cent	No.	Per cent	No.	Per cent
Below 99°	3	3.8	2	3.8	1	1.2
99.2°—100°	15	19.2	12	23.0	24	29.2
100.2°—101°	12	15.3	7	13.4	16	19.5
101.2°—102°	20	25.6	15	28.8	19	23.1
102.2°—103°	14	17.9	8	15.3	15	18.3
103.2°—104°	11	14.1	6	11.5	4	4.9
104.2°—105°	1	1.2	1	1.9	2	2.4
105.2°—106°	2	2.5	1	1.9	1	1.2
Total	78	99.6	52	99.6	82	99.8
Chill: Present	43	55.1	26	50	35	42.7
Chill: Absent	34	43.6	26	50	44	53.6
Chill: Not Noted	1	1.2	0	0	3	3.6
Total	78	99.9	52	100	82	99.9

Table XXV shows that in 160 transfusions (performed by the citrate method, for the most part) cases without any reaction that could be recognized were very rare, and that about half of the patients had a chill and a temperature over 101° F.

If nothing short of a severe chill, vomiting, hæmoglobinuria and signs of collapse be regarded as constituting a reaction, they are relatively infrequent, provided ordinary care is used in selection of the donor and in the actual technic of the transfusion. Granted that careful observations are made and that any elevation of temperature above 100° F. is considered an indication of a reaction, upon what do the reactions depend? It is believed that a variety of factors play a part.

More than one writer has expressed the belief—in which we concur—that many of the reactions are dependent upon changes which occur in the blood from the time it leaves the vein of the donor until it reaches the vein of the recipient; that these changes are inevitable and occur to some extent no matter what method is used, but are more marked when the so-called indirect methods are employed. This is not intended as a disparagement of any particular method, but it is our opinion that these changes, although often negligible from the therapeutic standpoint, are quite perceptible to the tissues of the recipient and would probably be sufficient to cause a recognizable reaction in a fair percentage of cases if the usual methods of transfusion were employed in refusion of a person's own blood. Reactions dependent upon such causes, although probably by far the most frequent, are usually mild or of only moderate severity. The really serious reactions, although more uncommon, are of much greater importance.

Those which concern us chiefly at the moment are such as may reasonably be attributed to incompatibility as reckoned by the standard of isoagglutination. Before passing to this aspect of the question, however, we wish to call attention to another phase which is usually overlooked. Most of us have a tendency to view transfusion as a ready means of correcting a deficiency in red blood cells, and so regard the material, administered intravenously, merely as a suspension of red cells, habitually disregarding the other ingredients or at least minimizing their importance. We rarely consider the fact that the patient receives plasma, leucocytes, and more or less damaged platelets, in addition to the needed red cells. Concerning the effect of the leucocytes not much evidence is available, but it has been shown that the platelet fraction may possess some toxicity.[23] The proteins in the plasma of transfused blood have been incriminated by Meleney *et al.*,[17] by Bayliss,[24] and by Bowcock.[25] Instances are occasionally encountered in which a second transfusion from the same donor results in the production of typical anaphylactic phenomena in the recipient after the injection of a very small amount of blood, despite the fact that the bloods of donor and recipient exhibit no evidence of isoagglutination either before or after the attempted transfusion. Such reactions differ markedly in type from those dependent upon agglutination. They have been observed in this hospital under the circumstances mentioned above, after the introduction of as little as 10 c.c. of blood. The character of the manifestations, the promptness with which they occur, the small amount of blood required to evoke them, all point to a protein as the cause and to the plasma rather than the red cells as the source. This phase of the problem urgently needs further study.

We now come to a consideration of the reactions dependent upon incompatibility resulting from isoagglutination. Such reactions are apt to be severe; occasionally they are fatal. Several instances of this sort are recorded and the manifestations are more or less characteristic. They occurred in a higher percentage of cases in the days before blood grouping came into general vogue, but still occur in spite of such precautions. It has been emphasized by many writers that mere grouping of patient and donor is insufficient to guard against this peril; that actual cross-matching may reveal agglutination in bloods assigned to the same group by the accepted methods. It is but natural to inquire how any incompatibility due to isoagglutination can exist between bloods of persons who really belong to the same group.

In the first place, the grouping may have been improperly carried out, not necessarily with defective technic but with poor reagents. The method in which II and III sera are used is the one most open to this criticism. Everything is staked upon the agglutinative power of these sera, often kept on hand as stock reagents and so capable of yielding misleading results unless the effect of deterioration is considered. We have titrated a considerable number of fresh sera and found, as others have done, a wide difference in agglutinative strength; one member of a group might agglutinate in a dilution of 1:30 or even higher, and another might not agglutinate beyond 1:2 or 1:4. If stored as stock sera, it is probable that the deterioration inevitable in both would produce a serious loss of potency in the weak more rapidly than in the strong serum. We have had the opportunity to check up actual incompatibilities between apparent members of the same group in which it was clearly shown that one or both of the stock sera used had lost much, if not all, agglutinative power.

In the next place, incompatibility may be obvious on matching the bloods assigned to the same group by means of tests quite free from criticism of this sort. This, as we have pointed out in earlier portions of this report, is dependent on the inherent limitations of the tests themselves. The mere fact that two bloods react in a similar manner to an arbitrary test which has only four possible combinations, does not prove that these bloods contain the same isoagglutinins and isoagglutinogens, and so belong to the same group. Practical experience has demonstrated the value of the added precaution which is afforded by direct matching of the bloods of donor and recipient, but if the accepted tests for grouping were infallible and there were really only four groups, the added precaution would be superfluous.

Severe reactions, of the type which we associate with isoagglutination, occasionally develop when no incompatibility has been revealed after the most careful grouping and cross-matching. Reactions of this sort are recorded as having occurred, not after a primary transfusion as a rule, but after the injection of blood from a donor whose blood had been used for the same patient without ill effect on one or more previous occasions. In some non-fatal cases of this kind, subsequent tests of the blood of donor and recipient have shown agglutination of the donor's cells—sometimes with hæmolysis as well—by the serum of the recipient. Under these conditions it has been natural to assume that the earlier preliminary tests must have been incomplete or improperly performed. This has been the conclusion usually drawn in such cases, but it is not the only possible explanation.

Ehrlich and Morgenroth [26] were the first to show that immune isohæmolysins—but not autohæmolysins—might be developed in goats by the injection of the blood of other goats. Von Dungern and Hirschfeld [27] showed that immune isoagglutinins might be produced in the same way by the injection of dogs with the blood of other dogs. Experiments of this sort are considered to demonstrate the existence of an antigenic substance—hæmolytic receptor or agglutinogen—in the injected cells, different from that present in the cells of recipient,—a hæmolytic receptor or agglutinogen capable of producing by immunization a corresponding hæmolysin or agglutinin in the serum of the injected animal. It is quite possible that we may sometimes be repeating the essential features of these experiments in our repeated transfusions. If the red cells of the donor contain an antigenic complex—hæmolytic receptor, agglutinogen, or both together—different from that of the recipient, it is entirely within the range of possibility that we may eventually succeed in effecting an unpremeditated immunization, of very questionable value to the patient.

It may be asked how an agglutinogen could be present in the cells of the donor different from that in the recipient and yet escape detection in the preliminary matching and grouping. We must bear in mind, however, that the presence of an agglutinogen is revealed by its union with the corresponding agglutinin. It is this agglutinin—originally and naturally absent from the blood of the recipient—which may be developed by the process of immunization. An example may suffice to make this plain.

The blood of Group II (H.) has been shown to have the formula *A—b* and that of Group II (D.J.) the formula *A—bc*; in other words the bloods are alike except that one possesses an extra agglutinogen (*c*) not possessed by the other, (Sect. III, 3). By the ordinary methods of classification these bloods are both assigned to Group II. When they are matched against each other there is no agglutination. If H. were made the recipient and D.J. the donor in a series of properly spaced transfusions, it is quite likely that the blood of H. would develop immune isoagglutinin *C* in response to the repeated injection of the cells of D. J. containing isoagglutinogen *c*, and its formula would then become *AC—b*. When this stage was reached, another injection of blood having the formula *A—bc*—whether from D.J. or another—would surely result in a severe reaction. Examination of the two bloods at this time would reveal obvious incompatibility and the earlier tests would be discredited.

It is conceivable, however, that tests made too soon after such a reaction might fail to furnish evidence of isoagglutination. The supply of agglutinin *C* in the serum of the recipient might temporarily be depleted by absorption with the injected cells,—an absorption comparable to that considered responsible for the disappearance of

autohæmolysin following an attack of paroxysmal hæmoglobinuria.*

Thalheimer,[28] in commenting upon a case somewhat similar to, if not identical with the theoretical one we have just described says, "If the same donor is used for more than one transfusion on the same individual, the direct tests must be made each time before each transfusion. This is necessary because agglutinins may develop against a donor's blood when the donor is used more than once in the transfusion of the same patient."

In the same connection McClure and Dunn [29] say: "In the patients for whom many transfusions have had to be done, it has been observed that it is more and more difficult to find donors whose blood will match that of the patient. A donor may match perfectly early in the series of transfusions and later be found to be unsuitable. This is probably due to the development of iso-hæmolysins." [or of isoagglutinins?] "It is therefore most important that the bloods be matched before each transfusion."

A similar condition of affairs may explain reactions of the same sort following repeated injections of blood from Group IV, "the universal donor." Hooker and Anderson [21] have shown that the cells of one member of this group contained a specific antigenic substance capable of calling forth specific immune agglutinin in the blood of an injected animal. In Sect. VII we have pointed out that the observations of various workers concerning certain unusual members of Group IV can best be explained by assuming the presence in the cells of these exceptional bloods of an agglutinogen other than *a* or *b*. If such a Group IV blood with the formula *AB—c* were used for repeated transfusion of the same patient, no difficulty would arise after the first injection, perhaps not after the second or the third; but when immunization of the patient had occurred and agglutinin *C* was present in his serum,—whether it required one or a dozen injections to induce this condition—the next transfusion from the same donor or one with the same kind of blood, would surely produce a memorable result.

Other examples might be presented, but we feel that these two will suffice to illustrate the difficulties which may arise from the injection of red cells containing an agglutinogen not present in the cells of the recipient, even though the serum of the recipient is originally quite devoid of the corresponding agglutinin and so produces no agglutination when tested against the donor's cells. This we believe to be a matter of practical importance with a definite bearing upon the question of reactions following transfusion.

IX. Method of Procedure in the Classification of Isoagglutinin Groups

In the preceding sections we have presented the reasons for our belief that the usual methods for classification of blood groups are unsatisfactory, in that they fail to yield all of the information needed. We feel that this criticism is just, but inadequate, unless accompanied by constructive suggestions calculated to remedy the obvious deficiency. In the present incomplete state of our knowledge concerning isoagglutinin groups, however, it is not a simple matter to evolve a scheme capable of meeting every contingency; nevertheless, we believe that existing conditions can be improved.

1. Selection of standard or test bloods.

A necessary preliminary requisite for accurate classification or grouping of unknown bloods is that great care be exercised in the selection and use of the standard or test bloods which are to serve as diagnostic reagents. There are four points which we may mention in this connection.

(*a*) Successive series of complete cross-agglutination tests, with 20 or more bloods in each series, are to be recommended as the initial step in the selection of the "known bloods" to be used in further study. Inclusion of the bloods of all persons constantly available, such as staff associates, laboratory assistants and the investigator himself, is desirable, as it is advantageous to have at hand ready sources of supply for the necessary test bloods.

(*b*) The agglutinin-agglutinogen content of the "known bloods" selected for the classification of others, should be ascertained. This may not be an easy task, and complete knowledge of the formulæ may not be obtained until the bloods have been in use for some time. Extensive cross-agglutination and absorption tests may be necessary to secure this information, but time so expended is not wasted. To place entire reliance on the results of blood grouping, it is essential that the standard or "known bloods" by which the others are judged, be really "known."

(*c*) For the classification of unknown bloods, it is preferable to use fresh serum and fresh cells from the "known bloods." We realize that this may not always be feasible, but do not consider that fact a sufficient reason for according the preference to stale reagents. If

* Are the quantitative relations between the blood volume of the recipient and the amount of blood received from the donor, such as to render this suggested depletion of agglutinin plausible? Ottenberg [13] has stated that under certain conditions one volume of cells can completely absorb the isoagglutinin from 16 volumes of serum. Considering the blood of donor and recipient as half cells and half plasma, a transfusion of 500 c.c. would contain sufficient red cells to absorb the agglutinin from 8 litres of blood. Calculating the blood volume at 1/13 of the body weight, we may assume for a patient of 65 kilos a blood volume of only about 5 litres. Even allowing for a very considerable reduction in the proportion of red cells and a corresponding increase in the relative amount of plasma in the blood of the recipient, the amount of red cells injected might be sufficient to "deplete" the agglutinin content, for the time being, rather markedly.

conditions are such as to necessitate the use of stored or stock sera, it is not impossible to utilize red cells, preserved according to the method of Rous and Turner [30] as stock reagents also.

(*d*) The "known sera"—whether fresh or stored—should possess good agglutinative titre, and the "known cells" should be readily agglutinable, at the time they are used for the classification of other bloods.

2. Recognition of agglutinins *A* and *B* and agglutinogens *a* and *b*.

In Section II, 6, it was pointed out that there are nine combinations of two agglutinins and the corresponding agglutinogens, which may be regarded as biological possibilities; and in Table XVI were shown the results which would be obtained with bloods representing these combinations when tested by different methods. It was seen that the four combinations considered to represent the four accepted groups, reacted consistently when tested by any or all of the different methods, but that the other five combinations gave different results depending on the type of test employed. It can also be seen from Table XVI that a discrepancy would be evident if any of these five combinations were tested by two methods properly selected. Thus each of the five combinations would give a result with method No. 1 (*x* r.b.c. vs. ser. II and ser. III), entirely different from that with method No. 2 (*x* ser. vs. r.b.c. II and r.b.c. III) and so would indicate at once an unusual blood. The same would be true if test No. 3 (*x* ser. vs. r.b.c. II; *x* r.b.c. vs. ser. II) were used in conjunction with test No. 4 (*x* ser. vs. r.b.c. III; *x* r.b.c. vs. ser. III). It is perhaps unnecessary to point out that what is actually accomplished by using tests No. 1 and No. 2 is exactly the same as with tests No. 3 and No. 4, namely, cross-agglutination of the cells and serum of the unknown blood with the sera and cells of Groups II and III, although the particular combinations used in the separate tests may lead to different interpretations (see Table XVI). Any unknown blood which gives discordant results with tests No. 1 and No. 2 —or with tests 3 and 4—is plainly an exception to the four accepted groups and merits further study before final classification or use in a transfusion. The next step in the investigation of such a blood is complete cross-agglutination tests with "known bloods" representing each of the four accepted groups. By this means one may classify an unknown blood according to its content in agglutinins *A* and *B* and the corresponding agglutinogens, but additional procedures must be employed if we are to ascertain with assurance the presence of agglutinin *C* and its appropriate receptor.

3. Recognition of agglutinin *C* and agglutinogen *c*.

The demonstration of an agglutinin requires an agglutinogen with which it can unite; the existence of an agglutinogen is proven by its union with an agglutinin. Both of these must exist to prove the existence of either, and one of them must be available to test for the presence of the other. So far as agglutinin *C* and its corresponding agglutinogen are concerned, our work has led us to believe that each of them is fairly widely distributed in human bloods. They have hitherto escaped recognition for two reasons; first, because the type of test in general use was not calculated to reveal anything unusual, and second, because a simpler explanation sufficed to account for the behavior of most bloods when subjected merely to cross-agglutination tests, and also the behavior of the relatively few bloods ever tested by the absorption method. The matter has been complicated, recognition postponed and rendered more difficult by the wide distribution of agglutinins *A* and *B* and their corresponding agglutinogens.

For the demonstration of agglutinin *C*, the most desirable test blood would be one with red cells containing only agglutinogen *c*, but bloods of this sort may be hard to find, as they are rather rare. We have not recognized an example of this type in our own studies, but patient No. 7627–š.J. reported by Janský, evidently had red cells containing a single agglutinogen which was neither *a* nor *b* (see Sect. VII, 1).

In the same way, the most direct method of showing the presence of agglutinogen *c*—either alone or in addition to another agglutinogen—is by means of a serum known to contain only agglutinin *C*. We have found two persons with blood of this sort, C.T. and G.V.C. (see Sect. IV, 1), but we have not gained the impression that bloods like these are common.

It may readily require considerable work to find an adult whose serum contains only agglutinin *C* or one whose red cells contain only agglutinogen *c*. The findings reported by Happ [18] (Sect. VII, 5) suggest that agglutinogen *c* may sometimes be present alone in the blood of infants for a period preceding the development of either agglutinogen *a* or agglutinogen *b*. If this is true, such a blood might be used for the demonstration of agglutinin *C* in other bloods.

Until one has discovered test bloods containing only agglutinin *C* or its corresponding agglutinogen, however, the question may be approached by a method less direct but equally decisive.

In Section III, 4, we have shown that bloods ordinarily assigned to Group II but having the formula *A—bc* are not very infrequent, as we found 13 in testing the bloods of 142 persons (9 per cent). We may estimate that about 40 per cent of the 142 bloods would be classified under Group II, and so may assume that in every 4 or 5 bloods considered as belonging to this group, one of them is likely to have the formula *A—bc*.

In Section III, 3, we have shown that certain bloods ordinarily assigned to Group IV, have the formula *ABC —o*. From our own work we cannot say whether bloods with this formula are more common than those with the

traditional formula, *AB—o*, but information gleaned from the tables published by Janský leads us to believe that they are, inasmuch as all of the 12 sera which he assigned to Group IV (Janský Gr. I) agglutinate the cells of the patient No. 7627–š.j. (see Sect. VII, I).

The accepted Groups II and IV are the common groups, including together about 83-85 per cent of persons in this part of the world.* Accordingly bloods containing agglutinin *C* (in addition to other agglutinins), and other bloods containing agglutinogen *c* (in addition to another agglutinogen), should not be difficult to find.

For the actual procedure we suggest that 20 bloods be selected, 15 of them representing Group II and the others Group IV. Absorb the serum from one of the members of Group IV with red cells from one of the members of Group II, and then test the absorbed serum against fresh cells from each of the 15 members of Group II. If this is not successful in differentiating the various Group II bloods into two types, absorb serum from the same Group IV blood with cells from another member of Group II, and so on through the entire list. One may then begin afresh with another Group IV serum, repeating the procedure until a serum is found which will completely agglutinate the corpuscles of a person apparently belonging to Group II, after that serum has been entirely deprived of agglutinins for the corpuscles of other persons classified in same group. When such a Group IV serum is found, it may also be deprived of all but agglutinin *C* by absorption with the cells of Group III, which will remove agglutinin *A*. This univalent serum may then be used for detecting the presence of agglutinogen *c* in other bloods.

The two types of Group II cells (*A—b* and *A—bc*) may likewise be used in the demonstration of agglutinin *C*. Any serum which agglutinates cells of the second type and not the first, contains agglutinin *C* but not agglutinin *B*. Any serum which agglutinates cells of both types, but which after absorption with the first type agglutinates only the second, contains both agglutinin *B* and agglutinin *C*.

With these test bloods the presence of agglutinin *C* and its corresponding agglutinogen may be demonstrated, and the information thus gained used to supplement the knowledge obtained by other means previously outlined for the detection of agglutinins *A* and *B* and their corresponding agglutinogens. Thus any of the 27 combinations of 3 agglutinins and 3 agglutinogens shown in Table XXIII may be identified.

With these test bloods also the search for sera containing only agglutinin *C* or red cells containing only agglutinogen *c*, will be greatly simplified. The fortunate finder of two such bloods has at his disposal means for ready recognition and classification of bloods representing any one of the 27 combinations mentioned above. In addition to the serum containing *C* and the cells containing *c*, there are needed two test bloods "known" to have the formulae *A—b* and *B—a*, in other words, a real Group II and a real Group III. An unknown blood may be classified as representing one or other of these 27 combinations if tested against these 3 sera (*A, B,* and *C*) and these 3 types of cells (*a, b,* and *c*). The results which would be obtained under these conditions require no table to make them clear. Agglutination of the unknown red cells by any of the 3 sera would indicate the presence of the corresponding agglutinogen in those cells; agglutination of any of the 3 types of red cells by the unknown serum would indicate the presence of the corresponding agglutinin in the unknown serum.

* The work of Liu and Wang,[31] Cabrera and Wade,[32] and the Hirschfelds,[33] seems to indicate that the relative frequency of the four accepted groups varies somewhat—perhaps considerably—in various races (not nations) of mankind.

4. Summary of procedure outlined.

The procedure recommended for the study and classification of isoagglutinin groups may be summarized briefly:

First, careful selection and use of test bloods, involving:

(*a*) A knowledge of their agglutinin and agglutinogen content.

(*b*) The use of fresh cells and fresh sera, if possible.

(*c*) The use of cells known to be readily agglutinable and of sera having good agglutinative strength at the time they are used.

Second, cross-agglutination of the unknown blood with:

(*a*) Cells and serum of a blood having the formula *A—b*.

(*b*) Cells and serum of a blood having the formula *B—a*.

(*c*) Serum containingg only agglutinin *C*.

(*d*) Cells containing only agglutinogen *c*.

X. Comment

If our theme has been developed intelligibly, it will perhaps be evident to some that the classification of blood groups is not so simple, nor the number of groups so limited as has been generally believed. Presentation of what we believe to be facts can be the only justification for adding any complexity to a subject already explained to the satisfaction of a great many workers. The utility of blood grouping has been demonstrated by practical experience, but in our opinion its value might be considerably enhanced by more thorough knowledge of the actual agglutinin and agglutinogen content of the individual bloods. Entire elimination of isoagglutination, as a cause of post-transfusion reactions, would permit a more accurate evaluation of the other factors involved; this in turn we might confidently expect to be productive of improvements in technic that would decrease the undesirable results without detracting from the beneficial effect of intravenous administration of blood.

In this work we have examined blood from 200 persons during a period of three months, but the specimens from certain individuals were studied much more intensively than those from others. With the blood from these 200 persons we have performed 1282 macroscopic and 3570 microscopic tests, 4852 in all, of which we have records. This forms the basis of our report, but we do not consider it complete,—much remains to be done. It is published in the present unfinished state in the hope that others working in the same field may be induced to undertake experiments of a similar nature calculated to disprove or substantiate our work. Our object will have been partially accomplished if we succeed in calling attention to the fact that much remains to be learned concerning isoagglutination in human blood.

XI. Summary and Conclusions

The points which have impressed us in this work may be stated briefly.

1. The methods generally employed for blood grouping are based upon the assumption that there are only four isoagglutinin groups, and that the blood of every human being belongs in one of these groups. The tests based on this assumption are so devised as to cause each blood tested to fall into one or other of these four groups, thus serving to perpetuate a belief which no one has seriously questioned.

2. We have presented evidence that the popular belief concerning the existence of four and only four isoagglutinin groups is incorrect.

3. The presence of only two isoagglutinins and two isoagglutinogens in human blood is inadequate to explain our findings.

4. By direct tests and by absorption experiments, the existence of a third isoagglutinin and a third isoagglutinogen has been demonstrated. Although recognizing the possibility that there may be still other isoagglutinins and isoagglutinogens in human blood, we have found nothing thus far to indicate their existence; our observations have shown, however, that there are *at least* three of each.

5. With three isoagglutinins and three isoagglutinogens there are 27 combinations biologically possible.

6. We have found bloods corresponding to 8 of these combinations, and by citations from the literature have indicated the probable existence of a number of others.

7. Some of these combinations are undoubtedly more common than others; some may be excessively rare; others may not occur at all; it may not be possible to prove the existence of all of them.

8. We believe that these findings have a bearing of practical importance upon transfusion and furnish a plausible explanation for some of the hitherto unexplained post-transfusion reactions.

9. Allowance has been made for the possible occurrence of autoagglutination, which we believe has not been a complicating factor in our results.

10. The grouping of bloods should be determined on a basis of their agglutinin-agglutinogen content.

11. Only bloods with the same agglutinin-agglutinogen content belong to the same group.

12. Methods for the classification of blood groups have been suggested.

* * *

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JOSEPH R. DeLAMAR

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Joseph R. DeLamar, whose magnificent bequest to The Johns Hopkins University has made possible so much that otherwise could not have been undertaken in connection with the medical work of the institution, was born at Amsterdam, Holland, September 2, 1843. His father, a banker in Amsterdam, was of French origin, his mother Dutch. His father died when he was six years old. The boy seemed to have an uncontrollable love of adventure, and after his father's death he stowed himself aboard a Dutch vessel bound for the West Indies. When the young stowaway was discovered, he was put to work as assistant cook without wages. He later worked as a seaman until he was twenty years of age, and shortly after received a captain's command. He followed the sea for a number of years and visited almost every part of the world.

After the Civil War he conceived the idea that there was a substantial profit in wrecking and submarine work, which at that time offered large returns. He then abandoned the sea and entered upon the business of salvaging vessels, with headquarters at Vineyard Haven, Massachusetts, and operated along the entire coast to the West Indies. He was very successful in some of these undertakings. In 1872 he raised the "Charlotte," a transatlantic steamship loaded with Italian marble that had foundered off the Bermudas, thus accomplishing a result which had baffled the attempts of other wrecking companies. In this business he nearly lost his life in his personal attempt to examine the damage to the steamer "William Tibbitts," wrecked off Martha's Vineyard. In order to make this investigation it was necessary for him to put on a diving suit. For some unexplained reason he was imprisoned under water for a long time. This experience led him to abandon the business.

It was about this time, as he informed the writer, that he conceived the idea of salvaging anchors that had been cast away and lost in Vineyard Haven Sound. As everyone familiar with shipping knows, the waters in this locality are very shallow, the currents swift and the winter wrecks very numerous. The Captain, as he was invariably called in after life, knew that there were countless anchors in the shallow waters of the Sound, and he rigged up a schooner having a large and powerful magnet which he could throw from the stern and drag on the bottom. He then allowed the schooner to drift about the Sound, and when the magnet would indicate the presence of an anchor, it would be buoyed and subsequently taken aboard. In this way he succeeded in collecting a load of anchors, which he sold for a substantial sum of money.

He was also, at one time, engaged in trade in Africa. Operations by trading companies were then chiefly confined to the coast, most of the merchandise being brought from the interior to the coast on the shoulders of negroes,

Captain DeLamar decided to do trading in the interior. He equipped his company with a small cannon, a dozen blunderbusses, rifles and ammunition. He pushed into the interior as far as the depth of the rivers would permit, exercising constant vigilance to prevent attacks from hostile tribes. This venture was crowned with financial success. He traded principally on the Gambia and Great Jeba rivers. After three successful years he gave up this trade on account of the climate. Many of his crew died every year of various tropical diseases. He sold his outfit and business to an English company.

It was in 1878 that he conceived the idea of going into the mining business. He had accumulated a little money which he thought he could use to the best advantage in this way. He thereupon started for the West when the silver fever broke out in Leadville, Colorado, and visited a number of mines with a view of learning something about the mining business. He soon found that a mere inspection of mines and methods of mining would not prove of very great advantage to him if he were to pursue the mining business. At that time there was a mineralogist and geologist of some note in Chicago who was well known among the mining profession, and who devoted a part of his time to teaching. Captain DeLamar went to Chicago and asked him how long it would take him to teach him enough geology and mineralogy to enable him to recognize mineral-bearing rocks and also to make his own assays and analyses. The professor told him that the course was two years of a number of months each year. The Captain was impatient at the length of time required to instruct him and asked at once "Can't you complete my course in one year?" The Professor replied: "I can, if you will do the work." He said: "I will do the work and give you double pay." Which he did.

At the end of the year the Captain again proceeded to the West to pursue his intention of entering upon the mining business. While riding through the mountains he came across a number of miners who were engaged in developing a prospect. The Captain saw the ore on the dump and asked the men what they had. They professed ignorance of the mineral and of its value. The Captain recognized the ore as being similar to one of the samples that he had seen in the office of his teacher in Chicago, and that it was probably a valuable lead ore. He asked for a sample and took it across the mountain, made a little crucible of sand, smelted the ore and found, when he was through, that he had a very rich specimen of lead ore. He returned in a few days to the prospectors and bought their claim, which he developed and sold for a very substantial sum of money, thus laying the foundation for his subsequent large fortune.

He later discovered a vein of very rich gold and silver ore near Silver City, Idaho. This he developed very extensively before undertaking to sell the mine. It was due to his previous study at Chicago that he was able to recognize the great value of these ores. From this particular venture he made a profit of several million dollars.

From this time on throughout his life he was constantly interested in mines. The DeLamar-Mercur Mine of Utah was a development of his; also the DeLamar-Nevada Mine. The Nipissing Mines were at one time under his control and, as almost everyone knows, he was the one particularly responsible for the great development of the richest nickel mine in the world, now owned by the International Nickel Company. It was he who first recognized the possibility of large mining profits from low grade ores. He believed that many mines of low grade ores, then considered unprofitable to work, would pay if the production were large. He thereupon developed mines of this character, opening up and treating large quantities of ores per day, so that production was in large amounts. While the profit per ton was small, the quantity production yielded large profits. It was the principle of quantity production first applied to mining and in this he was a pioneer in the mining world.

The Captain's business career was characterized by great self-reliance, courage and sagacity; but his interests were not wholly confined to business and financial enterprises. His origin indicated his character, which was influenced both by his father and mother. To his father may perhaps be attributed his very decided artistic instincts and tastes. He was exceptionally fond of music and greatly enjoyed playing the beautiful organ in his own home. He also was at one time a skilful player of the violin. His chief interest in the latter years of his life was in the development of his country place on Long Island, where he made a wonderful collection of rare plants and flowers. His fondness for beautiful trees was displayed by his attention to arboriculture. So interested was he in this that he would purchase a full-grown and beautiful tree almost anywhere he could find it and pay any price that might be asked for it. In the later years of his life he also developed a decided taste for art in the form of paintings and sculpture. In the collection of these his taste was catholic. His residence in New York was filled with objects of art of all kinds and descriptions, many of them of great value.

In 1891, while living in Idaho, he served as a State Senator in the first Legislature of that State. He was offered the United States Senatorship, which, however, he did not accept.

Captain DeLamar died in the City of New York, December 1, 1918, and after providing under his will for his daughter and only child, Miss Alice Antoinette DeLamar, made Harvard University, Columbia University, and The Johns Hopkins University his residuary legatees. The provisions of his will affecting the use of the legacies to the residuary legatees are remarkable for broadmindedness and wisdom, and for the confidence which they repose in the beneficiaries of his bounty. The purposes to

which his legacies are to be put and the methods which the legatees may adopt in realizing those purposes are set forth in his will as follows:

"To provide for the study and teaching of the origin of human disease and the prevention thereof, and for the study and teaching of dietetics and of the effect of different foods and diets on the human system and how to conserve health by proper food and diet; and in connection with the foregoing purposes to establish and maintain professorships, instructorships, scholarships and fellowships: to construct, maintain and equip laboratories, clinics, dispensaries and other places for such study and research and to provide for the proper housing of the same: to publish and disseminate the results of such study and research not only in scientific journals and for physicians and scientists, but, also, and this I do especially enjoin on said legatees, by popular publications, public lectures and other appropriate methods to give to the people of the United States generally the benefits of increased knowledge concerning the prevention of sickness and disease and also concerning the conservation of health by proper food and diet.

"In aid of the foregoing purposes the said beneficiaries may respectively use any means which from time to time shall to them, respectively, seem expedient, including research, publication, education, the establishment and maintenance of charitable, educational or benevolent activities, agencies or institutions appropriate thereto and the aid of any other such activities, agencies or institutions already established or which may hereafter be established.

"It is my hope that my said residuary legatees will be able to keep the principal of the bequest to them severally made intact and that they will be able by the proper investment thereof to accomplish the foregoing purposes by the use of the income therefrom, but I do not place any limitations on their right to use the principal of such bequests for the purposes above named, should they or any of them desire to use the principal of the same for such purpose or purposes."

The universities to which his gifts were made have up to the present time each received $3,528,000. Few individuals in this or any other country have made such munificient bequests to medical education as did the late Captain DeLamar. Not many benefactors of education of any sort have shown the wisdom he exhibited in relieving his beneficiaries from hampering restrictions, which sometimes so limit the freedom of action of those entrusted with the administration of such bequests and consequently diminish the possibility of efficient action.

Captain DeLamar's name will not only forever be associated with The Johns Hopkins University, it will also figure always as that of one who has contributed in an extraordinary measure to the promotion of scientific medicine in the United States.

BOOKS RECEIVED

Ten Talks to Girls on Health. For Club Leaders. By Augusta Rucker, M.D. 1921. 12°. 99 pages. The Woman's Press, New York City.

University of Illinois, College of Medicine, Chicago. Collected Studies from the Department of Pathology and Bacteriology. Volume V, 1920-21.

The Mechanism of the Brain and the Function of the Frontal Lobes. By Professor Leonardo Bianchi. Authorized translation from the Italian by James H. MacDonald, M.B., Ch.B., F.R.F.P.S. (Glasg.). With a foreword by C. Lloyd Morgan, LL.D., D.Sc., F.R.S. 1922. 8°. 348 pages. William Wood & Company, New York; E. & S. Livingstone, Edinburgh.

Philadelphia Academy of Surgery. Transactions. Volume XXII. 1922. 8°. 202 pages. Printed for the Academy, Philadelphia.

Respiration. By J. S. Haldane, M.D., LL.D., F.R.S. 1922. 8°. 427 pages. Yale University Press, New Haven; Humphrey Milford, Oxford University Press, London.

Oxford Medical Publications. Publishers: Henry Frowde, London; Hodder & Stoughton, London. The following five volumes:

—*A Treatise on Glaucoma.* By Robert Henry Elliot, M.D., B.S. (Lond.), Sc.D. (Edin.), F.R.C.S. (Eng.). With 213 illustrations and frontispiece. [Second Edition.] 1922. 8°. 656 pages.

—*The Clinical Method in the Study of Disease.* By R. M. Wilson, M.B., Ch.B. With a biographical note on the life of Dr. Horace Dobell. 1921. 12°. 57 pages.

—*The Principles of Electrotherapy, and Their Practical Application.* By W. J. Turrell, M.A., D.M., B.Ch. (Oxon.), D.M.R. & E. (Cantab.). 1922. 8°. 276 pages.

United States Life Tables, 1890, 1901, 1910 and 1901-1910. Explanatory Text, Mathematical Theory, Computations, Graphs, and Original Statistics, also Tables of United States Life Annuities, Life Tables of Foreign Countries, Mortality Tables of Life Insurance Companies. Prepared by James Glover. 1921, 4°. 496 pages. Government Printing Office, Washington.

Diagnostic, Traitement et Expertise des Séquelles des Blessures et des Accidents des Régions Maxillo-Faciales. Traitements Chirurgicaux, par Léon Dufourmentel. Traitements Prothétiques, par Léon Frison. Préface par P. A. Gilbert. 1922, 12°. 151 pages. J. B. Baillière et fils, Paris.

Potter's Compend of Human Anatomy. Revised by D. Gregg Metheny, M.D., L.R.C.P. and S. (Edin.), L.F.P.S. (Glasgow) Eighth Edition, with 139 illustrations; also numerous tables and 16 plates of the arteries and nerves. [1915,] 16°. 430 pages. P. Blakiston's Son & Co., Philadelphia.

Principles and Practice of X-Ray Technic for Diagnosis. By John A. Metzger, M.D. With 61 illustrations. 1922, 8°. 144 pages. C. V. Mosby Company, St. Louis.

Dietetics for Nurses. By Fairfax T. Proudfit. Second edition, completely revised. 1922, 8°. 524 pages. The Macmillan Company, New York.

Diseases of the Skin. By Henry H. Hazen, A.B., M.D. Second edition, with two hundred forty-one illustrations, including two color plates. 1922, 8°. 608 pages. C. V. Mosby Company, St. Louis.

The Harvey Lectures. Delivered under the Auspices of the Harvey Society of New York, 1920-21. By Dr. Jacques Loeb, Prof. Jules Bordet, and others. Series XVI. 1922. 8°. 235 pages. J. B. Lippincott Company, Philadelphia and London.

College of Physicians of Philadelphia, Transactions. Third series, volume forty-third, 1921, 8°. 558 pages. Philadelphia.

Bibliography of Hookworm Disease. Publication No. 11. 1922. 8°. 417 pages. The Rockefeller Foundation, International Health Board, New York City.

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The Treatment of Fractures. With Notes upon a few Common Dislocations. By Charles Locke Scudder, M.D. Ninth edition, revised, with 1252 illustrations. 1922, 8°. 749 pages. W. B. Saunders Company, Philadelphia and London.

The Elements of Scientific Psychology. By Knight Dunlap. Illustrated. 1922, 8°. 368 pages. C. V. Mosby Company, St. Louis.

Physical Diagnosis. By W. D. Rose, M.D. Third edition. Three hundred nineteen illustrations. 1922. 8°. 755 pages. C. V. Mosby Company, St. Louis.

Physiology and Biochemistry in Modern Medicine. By J. J. R. Macleod, M.B. Assisted by Roy G. Pearce, A. C. Redfield, and N. B. Taylor, and by others. Fourth edition. With 243 illustrations, including 9 plates in colors. 1922, 8°. 992 pages. C. V. Mosby Company, St. Louis.

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The Medical Society of London. Transactions. Volume forty-fourth. Edited by Sir William Henry Willcox, K.C.I.E., C.M.G., C.B., M.D., F.R.C.P. and Herbert W. Carson, F.R.C.S. 1921, 8°. 301 pages. Printed for the Society, London.

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Injury, Recovery, and Death, in Relation to Conductivity and Permeability. By W. J. V. Osterhout. 1922, 12°. 259 pages. Monographs on Experimental Biology. J. B. Lippincott Company. Philadelphia and London.

Animal Parasites and Human Disease. By Asa C. Chandler, M.S., Ph.D. Second edition, revised. 1922, 8°. 572 pages. John Wiley & Sons, Inc., New York; Chapman & Hall, Limited, London.

The Causes of Heart Failure. By William Henry Robey. 1922, 16°. 45 pages. Harvard University Press, Cambridge.

Rickets. A Study of Economic Conditions and their Effects on the Health of the Nation, in two parts combined in one volume, freely illustrated. By J. Lawson Dick, M.D. Ed., F.R.C.S. Eng. 1922, 8°. 488 pages. E. B. Treat & Co., New York.

Clinical Medicine. I. Tuesday Clinics at the Johns Hopkins Hospital. By Lewellys F. Barker, M.D., LL.D. Illustrated. 1922, 8°. 617 pages. W. B. Saunders Company, Philadelphia and London.

Diseases of Women. By Harry Sturgeon Crossen, M.D., F.A.C.S., Fifth edition, revised and enlarged. With nine hundred thirty-four engravings, including one color plate. 1922, 4°. 1005 pages. C. V. Mosby Company, St. Louis.

The Biology of Death. Being a Series of Lectures Delivered at the Lowell Institute in Boston in December 1920. By Raymond Pearl. Monographs on Experimental Biology. 1922. 8°. 275 pages. J. B. Lippincott Company, Philadelphia and London.

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Arab Medicine and Surgery. A Study of the Healing Art in Algeria. By M. W. Hilton-Simpson, B.Sc. 1922. 8°. 96 pages. Oxford University Press, London.

Text-Book of Pediatrics. Edited by Professor E. Feer. Translated and edited by Julius Parker Sedgwick, B.S., M.D. and Carl Ahrendt Scherer, M.D., F.A.C.P. 262 illustrations. First edition in English. 1922, 8°. 917 pages. J. B. Lippincott Company, Philadelphia and London.

Clinical Symptomatology of Internal Diseases. Part 11. Generalized Pain. By Prof. Dr. Norbert Ortner. Only authorized translation into the English language of the 2nd German edition. By Francis J. Rebman. With an introduction by Thomas Webster Edgar, M.D. 1922, 8°. 596 pages. Medical Art Agency, New York.

Obstetrics for Nurses. By Everett Dudley Plass, M.D. 1922, 8°. 410 pages. D. Appleton and Company, New York and London.

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Ophthalmoscopy, Retinoscopy and Refraction. By W. A. Fisher, M.D., F.A.C.S. With 248 illustrations including 18 colored plates. 1922. 12°. 218 pages. W. A. Fisher, Chicago, Illinois.

An Introduction to the Practice of Preventive Medicine. By J. G. Fitzgerald, M.D., F.R.S.C. Assisted by Peter Gillespie, M.Sc., C.E., M.E.I.C. and H. M. Lancaster, B.A., B.Sc., and chapters by Andrew Hunter, J. G. Cunningham, and R. M. Hutton. With appendix articles by various contributors. 1922. 8°. 826 pages. C. V. Mosby Company, St. Louis.

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Foundations of Biology. By Lorande Loss Woodruff. 1922, 12°. 476 pages. The Macmillan Company, New York.

Montaigne and Medicine. Being the Essayist's Comments on Comtemporary Physic and Physicians; his Thoughts on Many Material Matters Relating to Life and Death; an Account of his Bodily Ailments and Peculiarities and of His Travels in Search of Health. By James Spottiswoode Taylor, Commander, Medical Corps, U. S. Navy, M.D., F.A.C.S. 1922, 8°. 244 pages. Paul B. Hoeber, New York.

History of American Red Cross Nursing. By Lavinia L. Dock, R.N., Sarah Elizabeth Pickett, B.A., Clara D. Noyes, R.N., Fannie F. Clement, B.A., R.N., Elizabeth G. Fox, B.A., R.N. and Anna R. Van Meter, B.A., M.S. Illustrated. 1922, 8°. 1562 pages. The Macmillan Company, New York.

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The Writing of Medical Papers. By Maud H. Mellish. 1922. 16°. 157 pages. W. B. Saunders Company, Philadelphia and London.

Remembering and Forgetting. By T. H. Pear, M.A., B.Sc. With nine diagrams. 1922. 12°. 242 pages. E. P. Dutton and Company, New York.

The Successful Physician. By Verlin C. Thomas, M.D. 1923. 8°. 303 pages. W. B. Saunders Company, Philadelphia and London.

An International Congress of Ophthalmology. Held Under the Auspices of the American Ophthalmological Society. The Section on Ophthalmology of the American Medical Association. The American Academy of Ophthalmology and Oto-Laryngology, April 25-28, 1922. 8°. 713 pages. Washington, D. C.

Medical Psychology and Physical Research. By T. W. Mitchell, M.D. 1922. 12°. 244 pages. E. P. Dutton and Company, New York.

American College of Surgeons. Tenth Year Book. 1923. 8°. 807 pages. Chicago.

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Oxford Medical Publications. Publishers: Henry Frowde, London; Hodder & Stoughton, London. The following three volumes:

Clinical and Operative Gynæcology. By J. M. Munro Kerr. 1922, 8°. 832 pages.

The Heart as a Power-Chamber. A Contribution to Cardio-Dynamics. By Harrington Sainsbury, M.D., F.R.C.P. 1922, 8°. 248 pages.

The Diseases of Children. Medical and Surgical. By The late Henry Ashby, M.D. (Lond.), F.R.C.P. and The late G. A. Wright, B.A., M.B. (Oxon.), F.R.C.S. Revised by Hugh T. Ashby, B.A., M.D. (Camb.), M.R.C.P. (Lond.) and Charles Roberts, M.B., B.S. (Lond.), F.R.C.S. Sixth edition, thoroughly revised and rewritten. 1922, 8°. 769 pages.

NOTES ON NEW BOOKS

The Anatomy of The Human Orbit and Accessory Organs of Vision. By S. Ernest Whitnall. (*London, Henry Frowde, & Hodder & Stoughton, 1921.*)

This Oxford Medical publication represents what is probably the most masterly and scholarly presentation of this subject which has yet been made. The book is divided into four sections dealing with osteology, the eyelids, the contents of the orbit and ophthalmic neurology. The first three sections are the most valuable. The illustrations of actual anatomical preparations are profuse, well chosen, and amazingly clear—a truly remarkable collection of photographs. A comprehensive bibliography is given.

The book will not only be of interest to the anatomist, but for the clinical ophthalmologist will fill a long felt need and be an invaluable reference work. It should be in the library of every ophthalmologist. A. C. W.

Morris's Human Anatomy. Edited by C. M. Jackson. Sixth Edition. 1921. $10.00. (*Philadelphia, P. Blakiston's Son & Co.*)

The sixth edition of Morris's Human Anatomy (the second to appear under the direction of C. M. Jackson) maintains the type of previous editions. Without great brilliance in any part, it is perhaps the most usable of current text-books for American students, the one in which more than in any other there is a gleam of modern analytical, functional anatomy. This character was already assumed by previous editions, and the sixth is not greatly changed, except in details, though there have been many shifts in the personnel of the contributors. Richard Scammon has contributed a new chapter on Developmental Anatomy, which comprises a clear review of the main facts of human embryology and a résumé of recent work on the growth of parts and organs. The older chapter on skin and ductless glands has been divided; the skin and mammary glands are now described by C. R. Stockard, in a sound account, however strange it may seem to find him cramped to the routine style of a text-book. J. F. Gudernatsch has revised the section of ductless glands. R. J. Terry has taken over the chapter on osteology from Peter Thompson, and that on the articulations from Wood Jones. His revision includes the use of some good radiographs. Dean Lewis now has the clinical and topographical anatomy; Elliott Smith, now the only English contributor, has done the special sense organs, and A. C. Eycleshymer the urogenital system. J. Parsons Schaeffer has revised the respiratory organs in the light of his long experience in teaching this field. One is glad to find the other chapters (digestive organs, lymphatic system, nervous system, blood-vessels, and muscles,) in the same competent hands as in the previous edition.

On the whole, one would like to find the contributors a little more free from the traditional mode of such works, and to see, at least, some of the *pontes asinorum* of anatomy (i. e., the development of the peritoneum, collateral circulation, the pelvic fascias, etc.,) so treated as to combine sound embryology and physiology with a truly graphic exposition; but a thorough criticism on this point would involve a discussion of the whole plan of anatomical text-books. Teacher and student will at least find this book a safe and conscientious reference work for the dissecting room. The illustrations remain a queer mixture of ancient and modern, and the printers have assailed the reader's eye with an incredible crudeness of color. G. W. C.

The Healthy Child from Two to Seven Years. By Francis Hamilton MacCarthy, M. D., Assistant Professor of Diseases of Children, Boston University. (*New York, The Macmillan Company, 1922.*)

This is an easily readable volume which has been published for the use of parents, nurses and workers for Child Welfare.

The author deals in an intelligent way with the dietary and hygienic control of the small child. He discusses the psychology of relationship between parent and child and offers many good suggestions.

In the last two chapters he gives a short review of the infectious diseases and minor ailments of childhood and offers a few simple remedies.

This book should be of use in the field to which it is assigned. J. H. B.

Brain Abscess. Its surgical pathology and operative technic. By Wells P. Eagleton, M.D. (*New York, The Macmillan Co., 1922.*)

Following a brief introduction pointing to the importance of a thorough clinical examination in any case of probable brain

abscess, the author gives a very short general review of the methods used in intracranial operations, without paying marked attention to the special features in suppurative processes within the cranium. These, however, are dealt with in the chapter on abscesses in the different fossæ. Etiology and clinical picture of abscesses in the anterior, middle and posterior fossa, together with the technic advisable in the different regions of the brain, are described very exhaustively, extensive use being made of the observations laid down in the current world literature and of an extensive personal experience. An accurate account of the surgical pathology in these cases, which forms the scaffold for any clinical differentiation renders the picture much more vivid. Detailed histories of cases give a good illustration of the characteristics in the different localizations of abscesses. In abscesses of the middle fossa the author, contrary to the generally accepted method, uses skin-bone-flap with an upper basis, instead of taking the bridge with the blood supply from the lower, temporal angle, which he utilizes for the dural flap. By using this method the danger of necrosis in the borders of the skin-flap becomes greater. The difficulty encountered in any case of brain abscess is to give a free drainage of the cavity for a sufficient length of time. The use of glass or rubber tubing is ineffective for the drainage and injurious to the brain substance. The brain tissue bulging forward into the place of decompression, the tube becomes buried in brain tissue. The collapse of the cavity leads to the formation of multiple, small abscesses. This is counteracted by using elder tubes with a hollow center, which will work their way out gradually without injuring the brain-substance. When a gauze packing is employed, the drainage of the cavity is restricted to a period of hours, a time too short to sterilize it, so that this technic is very often followed by multiple abscess formation.

For the understanding of the special features of abscesses in the different fossæ it would be much better if part III with the lucid summary of all data in surgical diagnosis of brain abscesses preceded the second chapter with the detailed surgical pathology and the suitable technic.

Two appendices with an analysis of 140 reported cases of frontal lobe abscesses and 125 necropsy findings of cerebellar abscesses are of inestimable value for the study of the variability of the clinical picture and the great variety of complications, which occur in the post-operative course and often jeopardize the final result. K. S.

A Treatise on Fractures in General, Industrial and Military Practice. By John B. Roberts, A. M., M.D., F.A.C.S. and James A. Kelly, A.M., M.D. Second Edition, revised and entirely reset. (*Philadelphia and London, J. B. Lippineott and Company.*)

One needs only a glance over the preface to be convinced that the authors have given a great deal of time and thought to their subject. Throughout the book one is impressed with the fact that there is no one and only method of handling fractures, but that the problem or problems presented in each case have many phases, and may be interpreted differently by different surgeons; that no two fractures, even though they may appear very similar, will necessarily yield to one and the same method of treatment.

The old principles that have held their own through years of applications have been happily blended by the authors with about all that has proven worthy among the new discoveries or contributions, as well as with a great many valuable methods long forgotten, but recently revived.

Too often it happens that fractures are looked upon as a solution of the continuity of bone and that only. The fact that there is a solution of continuity of a great many other structures is not always as obvious as most writers on the subject of fractures seem to imply. Of course, it may be clear in their own minds, but text-books are not written for the sole benefit of authors. Our authors have dealt with this phase of the question from the standpoint of diagnosis and treatment with unusual clarity of vision.

Chapters I and III under the heading of "General Considerations," are very expressive. Followed intelligently they should prevent many surgical disasters.

In popularizing early active and passive motion even to the point of removing splints carefully for that purpose and reapplying them, using care not to disturb fragments and guarding against undue tension when they are reapplied, the authors are contributing to a more rapid convalescence not only for the bone, but for the soft parts as well.

Not a few surgeons will refuse to subscribe to the statement that "While infection of bones is a serious condition, it should not follow a properly performed operation in the case of fractures any more frequently than after abdominal operations or procedures on other structures."

Although this attitude may be safe for the authors or for others equally skilled in the handling of fractures, it might lead one of less experience, but whose zeal exceeds his discretion, to undertake the open method in the treatment of fractures when in his hands the closed method would be far safer. In spite of the statement, however, the authors give such well balanced reasoning for the selection of fractures to be treated by the open method and those by the closed method that no one should be misled.

In this volume the authors have covered the fields thoroughly; they have included practically all that seems valuable among the new contributions; they have presented the subject briefly, though clearly, in a very convenient, attractive and readable form. They have confirmed the opinion of one reader at least that the care of fractures is fraught with the possibility of many perils protean in their aspects and unfortunately uncertain as to final results.

They have given us what ought to be a useful text-book for the student and one which should also serve as a sound guide later, when the responsibility of handling fractures may otherwise occasion him sleepless nights. E. H. H.

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